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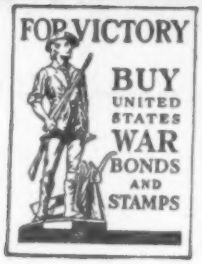

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THE MECHANISM OF RENAL COMPLICATIONS IN SULFONAMIDE THERAPY

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BROOKLINE, MASSACHUSETTS

THE ever-increasing number of case reports of renal complications in sulfonamide drug therapy indicates that neither the mechanism of their production nor the means of preventing them is yet understood. The following observations are offered in the hope that they may contribute to a better comprehension of this problem.

Early experience with sulfapyridine and sulfathiazole showed that it was mainly the insoluble acetyl derivatives of the drugs that crystallized in the urinary passages, producing obstruction and anuria. It was immediately obvious that a large urinary output would tend to keep these derivatives in solution and to prevent this complication. When sulfadiazine became available, it was predicted that the greatly increased solubility of acetylsulfadiazine in urine would be an important factor in such prevention,[1] but numerous reports in the literature show that this drug is by no means harmless in respect to the formation of crystals.

Various observers have described these crystalline sulfonamide deposits in the bladders, ureters, kidney pelves and tubules of patients who died of sulfonamide anuria, or who recovered when obstruction was relieved by ureteral catheterization. Similar lesions have been produced experimentally in animals by the use of large doses of the drugs.[2-4] When the crystalline deposits were not found in the ureters or kidney pelves at autopsy, it was assumed that they had been washed from the urinary tract before death. Gritty deposits noted on the cut surfaces — presumably within the tubules — of the kidneys of patients dying in anuria could usually not be demonstrated in microscopic sections because they had been dissolved from the tissues by the water and reagents used in preparing the sections. The finding of clefts suggesting that crystals had previously been present strengthened this belief. Subsequently various workers were able to prepare sections that demonstrated the obstructing concretions in situ in the renal tubules. It was believed that in all cases the kidney complications were due to such deposits.

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So far as can be determined, Long, Haviland, Edwards and Bliss[5] were the first to state that anuria in sulfonamide therapy may also be due to a true toxic injury of the kidney tubules similar to that seen in mercury bichloride poisoning. This was confirmed by Prien and Frondel,[6] who failed to find crystals in frozen sections of patients dying of sulfathiazole anuria. The histologic changes noted in these unobstructed kidneys were degeneration and focal necrosis of tubule cells and interstitial edema. Lederer and Rosenblatt[7] and Merkel and Crawford[8] described areas of focal necrosis in the kidneys and other organs and failed to find bacteria in these lesions; the changes in the kidneys included evidence of concretions and extensive tubular damage. Lyons[9] states that two types of renal complications occur — one a toxic effect on the tubules and the other a result of the precipitation of crystals. Sobin, Aronberg and Rolnick[10] have found focal necroses in human material that presented the clinical syndrome of sulfathiazole toxicity. Their conclusion that it has not been demonstrated that the renal changes in sulfonamide toxicity are independent of tubular obstruction by crystals seems justified.

NONOBSTRUCTIVE SULFONAMIDE ANURIA

The two following case reports are offered as evidence that uremia and anuria may occur without obstruction of the renal tubules or urinary channels by concretions and are presumably due to a true toxic injury of the kidney tubules.†

CASE 1.‡ A 39-year-old man developed pneumonia and was given 10 gm. of sulfathiazole in 24 hours. The temperature fell on the day after starting chemotherapy, and he became drowsy and perspired profusely. He failed to urinate on the 2nd day after the drug was started. He was catheterized, and the 480 cc. of concentrated urine obtained showed a large trace of albumin but no crystals. For the next 4 days the patient was intermittently comatose and responsive. The temperature was normal, and the pulmonic condition showed

†I am indebted to Dr. Monroe J. Schlesinger, pathologist of the Beth Israel Hospital, who studied the biopsied tissue of these cases critically and provided fresh autopsy tissue for studies of frozen sections.

‡I am indebted to Dr. George C. Prather and Dr. Ralph Volk for permission to study and report this case.

evidence of resolution. He received 2000 cc. of 10 per cent dextrose solution intravenously each day, but remained anuric except for 240 cc. of urine obtained by catheter on the 9th day after starting the drug. He was admitted to the Beth Israel Hospital the next day. He had passed a rigid life-insurance examination less than a year before.

In the hospital the patient was semicomatose, but could be aroused. Examination of the chest showed evidence of a clearing pneumonic process, which was confirmed by x-ray examination. The blood pressure was 124/75. There was tenderness to palpation over the right upper quadrant but none over the costovertebral angles. There was moderate edema of the lower back and lower extremities.

Of the three catheterized urinalyses recorded, the reaction was alkaline in two, and acid in the third. The specific gravity varied from 1.016 to 1.018, and the albumin from none to a heavy trace. There was no sugar. The sediment showed a few coarsely granular and hyaline casts, 10 to 30 leukocytes and none to 12 red cells per high-power field and many bacteria but no crystals. The blood counts were normal except for leukocytosis. The blood nonprotein nitrogen was 167 mg. per 100 cc.

On the 2nd hospital day, the nonprotein nitrogen rose to 190 mg. and the blood pressure to 190/130. The carbon dioxide combining power of the blood was 38 vols. per cent, and the blood chloride 440 mg. per 100 cc. *Staphylococcus aureus* was cultured from the urine. The patient received almost constant intravenous infusions of dextrose and normal saline solution up to 5300 cc. daily, but remained anuric except for small amounts of urine obtained by catheterization.

Late on the 2nd day, cystoscopy and retrograde pyelography were done. No concretions were seen in the bladder, and no obstruction was encountered by the ureteral catheters. The kidney pelves and ureters were poorly outlined in the pyelograms. It was thought that the kidney tubules were blocked by crystals, because no obstruction was demonstrated in the kidney pelves and ureters, and a rapid bilateral renal decapsulation was done under spinal anesthesia. Considerable edema was encountered in the flank muscles. The kidneys were enlarged, but the capsules were not so tense as had been expected. Tissue was taken by biopsy from the cortex of each kidney. There was no postoperative improvement, and the patient died the following day.

Microscopic examination of the biopsy specimens showed the glomeruli to be normal. The convoluted and collecting tubules were not remarkable except for small scattered focal areas of necrosis. These were represented by desquamation and breaking up of the lining epithelium of small groups of tubules, and by infiltration of a few polymorphonuclear leukocytes into these tubules. A diagnosis was made of multiple focal necroses of the kidney tubules.

Autopsy. The right kidney weighed 295 gm., and the left 285 gm. Both kidneys were much swollen. The remnant of the capsule stripped readily. The external surfaces were normal. The cut surface showed irregular grayish areas suggesting degeneration. The cortices measured 0.6 to 1.0 cm. in width and were sharply demarcated from the medullas, which showed similar but more marked degeneration. The calyxes, pelves and ureters were normal. No crystals or concretions were present.

Microscopic examination of the kidneys showed the glomeruli to be normal except for congestion in certain areas. The capsular spaces were empty. For the most part the convoluted and collecting tubules appeared normal. Widely scattered throughout the cortex and medulla were small groups of tubules that showed cloudy swelling and desquamation. In a few places the lumens of the convoluted and collecting tubules were irregularly filled with necrotic cellular débris and granular, hyaline and cellular casts. The interstitial tissue was not increased in amount and was infiltrated, sometimes densely, with lymphocytes and plasma cells adjacent to the degenerating tubules. An occasional polymorphonuclear leukocyte was seen. In the cortex these focal areas usually appeared to be adjacent to glomeruli. The focal tubular degeneration was less marked than in the biopsy sections taken 2 days before death, which suggested that the lesions had begun to heal.

The anatomic diagnoses were as follows: bronchopneumonia of the left upper lobe; acute bronchitis; bilateral renal decapsulation; kidney biopsy wounds; arteriolosclerosis of spleen; subacute passive congestion of liver; chronic duodenitis; congestion of the jejunum, ileum and stomach; subacute diffuse pancreatitis; focal necrosis of the adrenal glands; focal tubular degeneration of the kidneys; glandular hyperplasia of the prostate gland; congestion of the bladder; and hemorrhagic urethritis.

The second case is particularly interesting because it showed a pathologic process in the kidneys similar to that of the first case and because of the dramatic improvement following renal decapsulation.

CASE 2.* A 47-year-old housewife developed a temperature of 104°F. and was found to have an injected throat. Her physician gave her 20 gm. of sulfathiazole in 3 days. Her temperature was normal on the 4th day and she got out of bed. Six days later there was a recurrence of fever with sore throat. The patient received 32 gm. of sulfathiazole in 5 days. Antral puncture was done on the 6th day, and a small amount of pus was obtained. She voided little urine on this day and only 30 cc. in the next 24 hours. She was admitted to the Beth Israel Hospital.

The only significant findings on physical examination were an injected pharynx and tenderness on pressure over both kidneys, both anteriorly and posteriorly. The blood pressure was 140/80, temperature 100°F., the pulse 90, and the respirations 20.

Catheterized urines were uniformly alkaline before operation except for one specimen, which was acid; the albumin before operation varied from none to a trace. After operation the urine never showed more than a very slight trace of albumin and contained none 2 weeks later. There was no sugar. The urinary sediment before operation showed none to 20 leukocytes per high-power field but no drug crystals. The blood was normal except for a hemoglobin of 80 per cent (Sahli).

At entry the blood nonprotein nitrogen was 70 mg. per 100 cc., the carbon dioxide combining power 37 vols per cent, the chloride 390 mg. per 100 cc., and the sulfathiazole 2.3 mg. The nonprotein nitrogen rose to 100 mg. on the next day and remained above normal until 13 days after operation. The carbon dioxide combining power remained below 40 vols. per cent until 5 days after operation. A blood culture was sterile, and urine cultures were reported as positive for *Staph. albus.*

On the 2nd hospital day, the patient received 4000 cc. of 5 per cent dextrose and of normal saline solution intravenously; the urinary output was only 45 cc. On the 3rd day, she received 50 per cent dextrose and normal saline solution, the total volume being 2200 cc., and began to show signs of peripheral and pulmonary edema. The urinary output was 15 cc. Cystoscopy was done on the 4th day and showed nothing abnormal. Both ureters were catheterized with ease, and small amounts of urine were obtained. This was followed by decapsulation of the left kidney under cyclopropane anesthesia. A biopsy from the left kidney cortex was taken at operation. The kidney was somewhat swollen, but did not bulge after decapsulation.

The effect of renal decapsulation on the fluid balance was immediate and remarkable. On a fluid intake of 2200 to 4000 cc. daily for 3 days prior to operation, the urinary output was only 45 cc. 2 days before operation and only 15 cc. on the day before it. On the 1st postoperative day it was 410 cc., and on the next day it rose to 1200 cc., climbing to a peak of 6100 cc. 8 days after operation. The intake after operation varied between 1600 and 3400 cc., with a daily average of 2500 cc.

The temperature on the day of operation reached 101°F. and thereafter fell slowly by lysis to normal. A mild pneumonic process appeared 5 days postoperatively but was of no contributory significance. An intravenous pyelogram on the 20th postoperative day showed good excretion by both kidneys within 5 minutes of injection of the dye—a normal response.

The pathological report on the tissue removed at biopsy was similar to that in Case 1. The glomeruli and most of the tubules were normal. The degenerative process in the involved tubules was slightly more diffuse and appeared to be in a later, almost healed stage. The epithelium of the tubules appeared quite intact, and there was evidence of regeneration of tubule cells. The interstitial tissue showed infiltration of

*I am indebted to Dr. George Gilbert Smith for permission to study and report this case.

lymphocytes and plasma cells in the focal areas. The tubules were not dilated, nor was there evidence of crystalline material or pus. A diagnosis of focal tubular necrosis of the kidney was made.

It is well recognized that renal decapsulation for the relief of anuria fails in the great majority of cases, regardless of the cause of the condition. The polyuria after operation in this case, however, was too dramatic to be explained on the basis of gradual improvement characteristic of a healing process. The apparent success of decapsulation does not constitute an unqualified endorsement for its universal use in sulfonamide anuria.

The kidney tissues removed by biopsy and the fresh kidney tissue obtained post mortem in Case 1 were examined for crystals in the tubules. Frozen sections were cut and the sections removed directly from the microtome knife to a glass slide without preliminary floating of the cut section in water. Some difficulty was encountered in transferring frozen sections directly to glass slides without crumpling of the tissue. By freezing the microtome knife and the glass slide just before each cut was made, presentable sections were obtained. A drop of mineral oil — in which the sulfonamides are insoluble — and a coverslip were placed over the section, which was then examined with a polarizing microscope. Tissue detail was readily observed. No crystals were present in any of the sections. The frozen sections were correlated with formalin-fixed paraffin sections. This technic had previously been successfully used to demonstrate sulfonamide crystals in kidney tubules.[11] By the use of this method no crystals are lost from the tissues by solution because no solvents are used at any time.

The possibility that, in Case 1, crystals disappeared from the tissues after death and before frozen-section examination is also ruled out. By prior arrangement the kidneys were not washed or sponged at the autopsy table until blocks of fresh tissue had been taken for frozen sections. Furthermore, careful search of the urinary tract, from the renal papillas to the bladder, failed to reveal any crystals or concretions. In two other cases of sulfathiazole anuria with similar careful postmortem examination, no crystals were found anywhere in the urinary tract. This is supported by the failure to find crystals in the urine of nonfatal cases of sulfathiazole oliguria.[6, 12, 13]

It may be argued that the crystals were washed out by the urine after they caused the kidney damage and that the changes in the kidneys were not due to the drug. A number of relevant observations have been made.

Gross, Cooper and Lewis[2, 14] fed large amounts of sulfapyridine to rats for several weeks and noted the results. When the rats were killed at the end of the feeding period, they showed calculi in the urinary tract in a preponderance of cases; when the animals were allowed to live for ten days after administration of the drug was stopped, no calculi could be found, but there was dilatation of the tubules and other presumptive evidence that calculi had been present for a time. Presumably — it is so implied — it takes some time for calculi to be washed from the urinary tract after they are formed. What is most important, however, in so far as it bears on acute toxicity, is that calculi were found in the urinary tracts in *all* the rats that died during the period of drug administration.

A most instructive observation has been made by Lehr, Antopol and Churg.[15] They injected mice intraperitoneally with massive single doses of sulfathiazole and noted the location of its precipitation in the urinary tract. Depending on the time interval between injection and death of the animal, the precipitate was found in different parts of the tract. If death occurred within a few hours after the injection, the collecting tubules and papillary ducts were filled with a whitish material that extended into the pelves, ureters and bladder. After twenty-four hours the precipitate in the kidneys disappeared and the bladder became filled with white crystalline material that consisted almost entirely of free sulfathiazole. If the animals survived for at least several hours, anatomic signs of irritation were found in the kidneys — marked enlargement with congestion and edema. It appears that because of the extremely acute nature of the experiment these animals were able to flush their kidneys free of crystals before toxic damage to the renal epithelium produced oliguria, with resulting stagnation of crystals in the tubules.

If the findings of Gross, Cooper and Lewis are applied to the 2 clinical cases reported, it appears that both patients should have recovered spontaneously because their urinary tracts were found to be free of obstructing concretions when examined. Either obstructing crystals were never present or they were washed out before cystoscopy and biopsy were done. There is no reason to assume that the latter condition existed. After the onset of symptoms of uremia there was marked oliguria, and no crystalline precipitate was noted in the urine either before or after entry to the hospital.

If it is assumed that the areas of focal necrosis in the kidneys represent the damage done by transitory concretions, it is only logical to expect such damage to have been more pronounced in the collecting tubules[2–4] and, in the autopsy case, in the tubules of the renal papilla. The literature[2–4] records that in kidneys that contain crystalline deposits there is usually microscopic evidence of extensive tubular damage. But the tubular epithelium was intact in these locations except for the scattered foci that occurred throughout the entire kidney. The distribution of these foci did not correspond at all to the generally recognized localization of the tubular concretions. The objection that cortical biopsies do not give information on concretions located in the

medulla may be answered inferentially. Lack of evidence of tubular obstruction or damage of the collecting tubules in the cortex and the ready correlation of the biopsy and autopsy sections to show a consistent picture of a single lesion (focal necrosis) afford evidence that concretions were not present in the tubules of the renal pyramids.

It has been shown by numerous observers that uremic death may occur from tubular obstruction by acetylsulfathiazole concretions. It is agreed that temporary arrest of concretions in the urinary channels may produce kidney embarrassment and that such deposits may be washed out or dissolved if insufficient to produce uremic death in human beings before this clearing process is completed. But that extensive deposition of impacted crystals extending through the renal pyramids with accompanying anuria for several days will be relieved spontaneously seems doubtful.

If, in the 2 clinical cases, crystals had been present for a time only and had disappeared before the tissues were taken for study, some clinical improvement should have been manifested if the anuria was on a simple mechanical basis. It is a commonplace observation that temporary obstruction, as by a ureteral calculus, produces little kidney damage if there is no infection. The ability of the kidneys to clear themselves of crystals would be evidence of returning or surviving renal function. But in these cases the uremia became more profound with the lapse of time. It is possible that the persisting anuria was due to epithelial damage. In the absence of clinical or pathological evidence of concretions, it is reasonable to assume a primary chemotoxic cause for the focal lesions in the kidneys.

It may be objected that the changes in these kidneys were of a nonspecific nature and, together with the uremia, can be explained on the basis of toxicity due to the disease under treatment. This is unlikely. The picture is that of a transient focal degenerative process widely disseminated through the renal tubules and tending to heal without gross scar. Staphylococci were present in the urines of both patients, yet the lesions in the kidneys were not typical of such infection, nor did they suggest any other clinical condition. Furthermore, the uremia immediately followed the use of the drug. It has been produced experimentally in healthy animals by feeding sulfathiazole.

Dr. Schlesinger made an interesting observation concerning sequential relations in the biopsy and autopsy specimens. In Case 1 there appeared to be a definite progression in the degenerative and healing process, as evidenced by the sections taken at biopsy and at autopsy, two days intervening. The biopsy in Case 2 illustrates a later stage in the same healing process. The first patient received his initial dose of the drug nine days before the kidney was biopsied; the second patient received her first dose seventeen days before biopsy, or eight days earlier. In other words, the second patient's lesion appeared to show a healing stage eight days farther along than that of the first patient. No conclusions are drawn from this observation; it is merely offered as an interesting commentary.

Obstructive Sulfonamide Anuria

Although it is impossible to enlarge much on the causation of nonobstructive sulfonamide anuria beyond stating that it is probably due to a primary chemotoxic cause, much more can be said about the mechanism of the obstructive type of anuria. Prerenal factors, such as concentration of the drug in the bloodstream and excessive acetylation,[16,17] will not be discussed.

It is probable that crystals first form in the convoluted tubules of the kidney following concentration of urine by reabsorption of water. When deposits of insoluble acetyl derivatives are present, it is reasonable to assume that a supersaturated solution existed in situ or farther up the urinary tract. Scrutiny of the literature shows that there is no essential difference between sulfapyridine, sulfathiazole and sulfadiazine in the localization of the concretions.[2, 3, 12, 18–23] Furthermore, the presence of a single crystal is enough to "seed" a supersaturated solution and initiate mass crystallization. This happens in motionless solutions and is probably not strictly applicable to the urinary tract unless there is marked stasis.

The development of obstructing sulfonamide concretions from crystals in the kidneys is probably dependent on two physical conditions, the hydrodynamics of the urinary tract and the affinity of crystals for each other. The renal tubule empties its contents into the calyx in a manner analogous to the discharge of a slow-flowing river into a lake or other large body of still water. The discharge of the Mississippi River into the Gulf of Mexico provides a good analogy. Because of the disappearance of the current of the river at its mouth, suspended particles of mud and so forth are dropped, to form the well-known delta in the Gulf of Mexico. This formation builds up to such a height that the water flowing over it becomes very shallow and the fall or grade of the river becomes low. As a result, the current is slowed and deposition of suspended material occurs in the lower reaches of the river. Certain measures, such as dredging, are necessary to prevent the river from filling up and overflowing its banks.

In a similar manner the flow of urine through the renal tubule slows where the tubule empties into the broad expanse of the calyx. Not enough current remains to carry the suspended crystals onward. They are deposited in the calyx, impeding and then obstructing the flow in the terminal portions of the collecting tubules. The resulting stasis in the tubule serves to deposit more crystals. The tubules then fill with crystals in a retrograde man-

ner, the filling process progressing up the collecting tubules toward the convoluted tubules. Careful study of frozen sections in 5 cases has failed to show crystals in the collecting tubules (or higher) unless the terminal portions of these tubules were also filled with crystals. It is not necessary to assume that the pelvis or calyxes must be completely filled with crystals before the tubular deposition and obstruction can occur. Such has not been found to be the case. The building up of the delta at the mouth of the Mississippi River and the progressive silting of the lower river occur despite the fact that the Gulf of Mexico has not been filled up with sediment.

The early development of this process was observed in the kidney of an elderly patient who had received sulfathiazole for a massive pneumonia.[11] At autopsy the calyxes and pelvis of one kidney contained much crystalline material and there was a concretion blocking the ureter just above the bladder. Under the polarizing microscope acetylsulfathiazole crystals were found in the terminal portions of the collecting tubules, but there were no crystals higher in the collecting or convoluted tubules. No crystals were lost from the kidney tubules in preparation of the tissues because the previously described rigorous frozen-section waterless technic was followed.

The factor of crystal affinity is of great importance in the production of obstruction of the urinary tract. This is a surface-tension phenomenon. Crystals of the acetyl derivatives of the sulfonamides — and crystals in general — have an affinity for one another; and this causes them to adhere together to form aggregations or concretions. Anyone who has gently agitated a heavy suspension of crystals on a glass slide under the microscope and allowed the preparation to stand for a time has noted the familiar clumping of crystals.

The deposition of crystals in stagnant urine permits them to come in contact with each other to form concretions by simple aggregation. This may occur in the tubule, calyx or pelvis. Such masses of crystals then behave as ordinary urinary calculi, lodging in the kidney pelvis or the lower ureter or passing to the bladder when size permits. The readiness with which concretions form undoubtedly bears a relation to the number of crystals in the urine. The larger the volume of urine the less opportunity there is for the random collision and aggregation of crystals in suspension. If crystals are kept far apart, there is less tendency for concretions to form.

Prien and Frondel[6] examined the crystals in a series of 310 specimens of urine from patients receiving sulfathiazole therapeutically, and failed to find any correlation between the number of crystals in the urinary sediments and the presence or absence of evidence of renal irritation — oliguria, hematuria or albuminuria. The urines of certain patients suffering renal toxicity showed no crystals. On the other hand, the urines of most patients with extremely heavy crystalline deposits showed no evidence of renal complication. These urines had stood at room temperature for some hours, and the crystals did not appear until the urines had cooled to room temperature.

Crystalluria, as determined by the observation of ordinary cooled urines, is probably without significance unless there is oliguria, hematuria or other evidence of renal irritation. But, as Janeway[24] has pointed out, the presence of numerous crystals in freshly voided urine still at body temperature is extremely significant. The urinary concentration of the drug must be rapidly decreased by forcing fluids and either reducing or withholding the drug until the crystals disappear. Further therapy must be carried on with extreme caution.

The role of urinary stasis in the causation of concretions has been shown. Crystallization is favored in stagnant water. Residual bladder urine should be eliminated, whether due to cystocele, obstruction by the prostate or urethral stricture. Bedridden patients receiving large doses of the sulfonamides should be placed on urethral catheter drainage if the residual urine exceeds 60 cc.

Summary and Conclusions

Renal complications to sulfonamide therapy continue to occur despite an increasing experience and the use of the more soluble sulfonamide drugs. The usual mechanism that produces these complications is the obstruction of the urinary channels by insoluble concretions composed principally of the acetyl derivatives of the drugs. Less frequently, a toxic injury of the tubules, independent of concretions, produces anuria and uremia. In such cases the only lesion in the urinary tract may be a widely disseminated focal necrosis of the kidney tubules.

Two cases of sulfathiazole anuria and uremia are reported. No obstructing concretions were encountered in the ureters or kidney pelves by cystoscopy and pyelography. Renal decapsulation was done and cortical biopsies taken. One patient died. The other recovered rapidly, apparently as a result of decapsulation. There were no crystals or concretions in the kidney tissue taken by biopsy or in the entire urinary tract (including the kidney tubules) of the fatal case that came to autopsy. A rigorous technic is described that precludes the loss of drug crystals in preparation of tissues.

The most important factor in causation of renal complications is a low urinary output.

The development of obstructing concretions depends on two physical conditions — the hydrodynamics of the urinary tract and the affinity of crystals for each other.

Crystals of the sulfonamides first form in the convoluted tubules, where reabsorption of water occurs. Sedimentation of these suspended crystals

occurs in the terminal portions of the collecting tubules and in the renal calyx. Proximity of crystals here results in aggregation and the formation of concretions that obstruct the terminal portions of the collecting tubules. This process progresses in a retrograde manner up the collecting tubules. Calyxeal concretions remain in situ or pass down the ureter much as do ordinary urinary calculi.

1101 Beacon Street

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PRESIDENTIAL ADDRESS*

The Role of the Community Hospital in Postgraduate Teaching

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THE early meetings of this society were interrupted by World War I, and now another war disrupts its schedule. At the time of the last meeting the country was not at war, but everyone thought it soon would be. Selective service was already under way, and the Procurement and Assignment Service was in its last month of gestation. It was born in October, and then out of the blue December sky came the dastardly attack on Pearl Harbor, and war.

Through that winter and summer we had to adapt ourselves to dimouts, blackouts and air-raid alarms; the rationing of food, fuel and gasoline; the depletion and rearrangement of hospital staffs; and many other discomforts that made each approaching day uncertain and unpredictable. As the fall approached it seemed wise to the Executive Committee to postpone the prearranged meeting in Worcester. The fall of 1943 was no better, — in fact, conditions were worse, — and the meeting was again postponed. This year it was decided to chance a one-day meeting, and I am sure you will feel it has been successful.

Preparation for a world war to be fought on numerous fronts required the drafting of many millions of men from all walks of life. No groups were excluded by law except ministers of the Gospel and divinity students. The medical profession was, however, granted a privilege accorded no other group. The Procurement and Assignment Service — made up entirely of medical men, was set up by presidential decree and given quasi-official authority, at first under the Federal Security Agency and later under the War Manpower Commission. It was charged with the voluntary procurement of enough medical officers for the armed services, selected with careful thought concerning the needs of medical schools, hospitals and civilian care. The Army and Navy agreed not to commission any doctor who was not declared available for military service by the Procurement and Assignment Service. A heavy responsibility was courageously accepted by state chairmen and local committees. They have done their work well. Medical schools have been able to retain enough of their faculty members so that the teaching has not been too much curtailed. Hospitals have been able to maintain their staffs, — much depleted, to be sure, — and the quality of service has for the most part been kept fairly normal. Many retired members have gladly resumed their former positions. Many mistakes have been made. Some communities have suffered badly, particularly in the South, where

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many physicians volunteered before the Procurement and Assignment Service began to function. Some local communities have suffered through unexpected deaths. The Procurement and Assignment Service has undertaken to furnish replacements wherever possible, and several thousand have been accomplished so far. Between 50,000 and 60,000 out of an estimated 140,000 active physicians in the country are enrolled in the armed services today.

But this does not tell the whole story. There were 3156 deaths among physicians in 1943. About 6000 medical students will graduate this year with the accelerated program, but the great majority will go immediately into service, leaving only the physically unfit and a few women physicians for civilian practice. These will not be enough to replace those who die. But after this year even this number will be reduced, because the Army has cut its quota of students in medical schools from 55 to 28 per cent; the Navy quota remains at 25 per cent, leaving 47 per cent to be filled by physically disabled men and by women — an almost unattainable percentage. The Selective Service regulations refuse to allow the deferment of premedical students eighteen years of age or over and the entering classes this fall will probably be reduced 25 or 30 per cent. This is perhaps the most serious situation confronting the medical profession today. If the flow of students into the schools is not maintained, certainly not enough graduates will emerge at the other end. Much pressure has been brought to bear to change this ruling, even on the President himself, but to no avail. The Army and Navy maintain that the need of young men for combat service transcends every other requirement. A bill is now pending in Congress to amend the Selective Service Act so as to allow the deferment of premedical and medical students, but it is doubtful if it will prevail. The only hope is that the war in Europe will be over shortly, thereby lessening the need for so many medical officers and allowing at least some of the older ones to return to civilian practice. This the Army has promised to do promptly.

But the medical profession has not been allowed to determine its own policy in what is perhaps the most important thing of all — medical education. The accelerated program was practically forced on the medical schools by the military leaders. It allows no time for a breathing spell between semesters for the students to rest and assimilate what they have learned or for the overworked teachers to get their second wind. The 9-9-9 program for interns and residents, set up in the face of loud protests by the leaders in our profession, scrapped overnight the carefully worked out program of graduate training calculated to furnish adequate background for the practice of medicine and for training for the various specialties.

Only about 1000 men, representing one sixth of the graduates deferred for residencies, will have the least possible knowledge of any specialty. Of course, postgraduate instruction must be provided for these men. What form it shall take need not concern us here. Many minds and many committees are working on the problem. But what of the 3000 graduates who get only nine months of rotating internship? These men are the great source of concern at the present moment. Deplorable as the situation is, it confronts us, particularly those in hospitals not connected with medical schools. We must exert ourselves to the utmost to give these boys all they can take in nine months.

This leads naturally to certain thoughts I have in mind concerning hospitals — those of approximately 150 beds or over not connected with medical schools in the New England cities. There are about fifty of these, representing over 12,000 beds.

It is a trite remark that a hospital is an integral part of a community, and that the community should recognize its responsibility to support it. A hospital is made up of three parts — the trustees, the administration and the medical staff. No two of these can function without the third, and there should be a most cordial and sympathetic relation between the three; there should be no pulling at cross purposes. The trustees should take the staff as much as possible into their confidence; they should seek to know the various staff members and to understand their viewpoint, which is so often different from the layman's. A definite liaison should be set up between the two bodies through an intermediary unit — an executive committee, staff council or what you will. This should consist of certain members elected by the staff — not too large to be unwieldy but large enough to be representative of the various services. The director of the hospital should be an *ex officio* member. Meetings should be frequent, with a frank exchange of ideas and opinions that will prevent many unpleasant episodes that weaken the *esprit de corps* of the hospital.

I said that a community should recognize its responsibility to the hospital. Do hospitals always recognize their responsibility to their communities? This consists primarily in furnishing the best possible medical care. The first requisite for good medical care is a well-organized medical staff. This is a requirement under the minimum standard for approval as a Class A hospital set up by the American College of Surgeons. There should be a chief of staff or a chief of each service; this also is a minimum requirement. But it should be required that the Chief be given definite authority, and that he be chosen for his leadership, enthusiasm and ability to use his authority courageously and tactfully. Seniority should never be the deciding factor in his selection.

One often hears the distinction made between a teaching and a nonteaching hospital. This is wrong. Every hospital should be a teaching hospital. Someone can always be found to teach, if there are

no interns — try it on the nurses. Remember teaching is like Portia's "mercy": "It is twice bless'd: It blesseth him that gives and him that takes." But teaching in a hospital requires leadership; you would not have a school without a master or a medical school without a dean. A teaching hospital will not function without a chief. Rotating services without the continuity provided by an active chief are outmoded, yet how many hospital staffs have just that, with a chief on paper?

Daily ward rounds should be regular and punctual, be conducted with decorum and be attended by all the members on service at the time. Casual rounds at all hours are demoralizing for nurses and interns alike. I know of a hospital where the visiting surgeon makes rounds whenever he chooses, and the assistant likewise. If they happen to meet, well and good; if not, assignments to operate or questions of treatment are communicated by telephone. Is it small wonder that this hospital has difficulty in getting good interns. Unfortunately, this situation can probably be duplicated many times. There should be free discussion of interesting cases at the time of the visit, not necessarily at the bedside, which may be unwise in small hospitals where gossip travels on invisible wings. The intern should be given a chance to state his views.

The minimum standard requires certain qualifications for staff membership. They are not enough. Every new member of the staff should be seen by the chief or by a staff committee and informed what his privileges as a member are at the moment and what they may be expected to be in the future. Qualifications for every step in the professional ladder should be explicitly set down in writing. It should be distinctly understood at the start that promotions are made on merit, not by seniority. If this is clearly understood when a man accepts membership on the staff and signs the bylaws, many future unpleasant episodes will be avoided. On the other hand, the younger members of the staff should not be left to their own devices, but should be encouraged to progress by special ward work, regular reading or discussions of cases.

In many hospitals, men are not restricted in their care of private patients, so that they can attempt operations or treat illnesses that they would not be allowed to do on ward service. This applies to the so-called "courtesy staff." If a man is not considered competent to undertake a ward service, he should not be allowed unrestricted privileges for his private cases. This is becoming more important with the increasing popularity of the Blue Cross and other insurance schemes, which tend to remove patients from ward service to a semiprivate status.

A well-organized staff presupposes a proper laboratory and x-ray facilities, adequate clinical records and the correct use of case-history teaching in regular clinical conferences. These conferences are of great value. If they are held at the same day and hour each week, the habit of attendance is soon formed. If they are sporadic, the attendance will be likewise. A few full-time men, such as a pathologist, a radiologist and an anesthetist, form an excellent nucleus for such an organization. An essential part of every hospital is a good working library, with its nucleus the weekly, monthly and quarterly medical periodicals, so arranged that they can be easily consulted. The *Quarterly Cumulative Index* should occupy a prominent place. An interested staff member should be in charge as librarian, and books of reference should be carefully chosen, with due regard to the various branches of medicine. The trustees should be made to see the wisdom of setting apart adequate physical quarters for such a library, quiet and off the beaten line of travel. An intern — or a staff member, for that matter — cannot be expected to read studiously unless he is given a proper place in which to read.

It is not always realized how much this kind of setup means to a hospital. In the first place, it makes all the difference in the world in getting a quota of good interns. Even before the war there were not enough interns to go around, and naturally they chose the hospital with a reputation for good service and good training. There seems to be an underground method of communication among prospective interns. Again, the public does not realize how much this type of organization means to the community. I do not believe that the trustees realize it, or they would do more to bring it about. The more efficient hospital facilities are, the more incentive there is for young medical graduates to settle in the community. Hospital opportunities are considered a necessity today, and men look the hospital situation over carefully before deciding where to start practice. This is going to be even more so as men come back from service, having little or no idea where they want to practice.

Now all this requires tactful leadership and sympathetic co-operation; it also requires the active support of a well-informed board of trustees. Yet it is not unattainable in any of the New England hospitals.

There are small hospitals in many communities that cannot fulfill all these requirements. They cannot be expected to provide equipment for elaborate medical or surgical procedures or to furnish adequate laboratory and x-ray facilities. It is often possible for a hospital of this kind to co-operate with a neighboring, larger and better-equipped hospital, to the mutual advantage of both. Periodic laboratory and x-ray service can be furnished by the larger institution, and complicated medical or surgical cases can be transferred to it from the smaller hospital without prejudice if its staff is given appropriate appointments in the larger hospital. The Salem Hospital has an extremely satisfactory agreement of this kind with the Mary Alley Hospital of Marble-

head, and to a lesser degree with the Cable Memorial Hospital at Ipswich.

The American Board of Surgery has set up an admirable curriculum for the training of surgeons, but the diplomats of this body will be spread out rather thin for many years to come. We of the New England Surgical Society are diplomats, but do we do all the surgery for New England? I venture to say that we do only a small fraction of it.

There are not residencies enough to accommodate all the graduates who desire to continue surgical training. Of thirty-three hospitals in New England with 200 beds or over, which might be considered large enough to furnish adequate clinical material for a resident, only nine are approved for residencies, and not all these are surgical. Most of the hospitals could provide excellent training for a resident in surgery if they would organize their staffs in some such manner as I have indicated. These hospitals represent almost 7000 beds, a fair proportion of which are assigned to surgical patients. The criticism is often raised that having a residency interferes with intern training. I do not believe that this is true. An intern should have at least eighteen months of rotating service. This will give him perhaps six months of surgery, including urology and orthopedics, but not enough to permit him to do major operating. Furthermore, the supervision and assistance a resident can give an intern is invaluable.

It is also said that a resident takes away work from the younger staff members. If the work is properly arranged this should not be so. The resident can be of great assistance with private patients, who present a field of training largely ignored in many hospitals. It is just as proper to use private patients in teaching, as it is ward patients, provided that it is done wisely. The old apprentice system certainly used private patients to good advantage. It taught the young doctor something about the art of medicine as well as about the science of medicine. How can he learn this better today than by accompanying the older surgeon on his private visits? This type of training is badly needed. So many young men know all there is to know about a given disease but nothing whatever about the personality that happens to harbor that disease.

One fault that must be overcome is the tendency for men who have been residents in hospitals in large teaching centers to feel that they must remain there indefinitely. Many must and should remain, of course — but there are certainly others who can go out into small communities to practice surgery, to their own advantage as well as that of the community. They should not do so in the expectation that they will immediately become chiefs and do all the surgery. This thought invites disaster. They need not be ashamed to take a humble position on the staff, sell their talent to their associates, and work their way up to become leaders. Such men, if they are patient and tactful, can eventually build up a strong organization in almost any hospital. There is an immense amount of satisfaction in creative work. You who are associated with graduating residents can do much to encourage this migration.

The value of some sort of group practice has been proved beyond reasonable doubt. It is not possible to organize a private group clinic in every community; indeed, in many it may be extremely unwise. It is possible, however, to establish an informal group in many of these hospitals. If a sincere effort is made to encourage men to fill the various specialties, a reasonably complete staff can be developed. If the laboratory and x-ray setup is good and frequent consultations are encouraged, resident patients at least may have the advantage of group practice.

We should look forward to the day when all the doctors on the active staff of a hospital will have their offices in the hospital, or near enough to it for them to use its facilities easily for their ambulatory patients. This would represent a substantial economy to physicians and patients alike, in both time and money.

The need of greater supervision in surgery as well as in teaching is clear. It is so easy to master the technics of operations; it is so difficult to acquire the much more necessary surgical judgment.

You may say that I am addressing these remarks to the wrong audience. You may say that all the hospitals in which you are interested fulfill these qualifications. Be this as it may, there are many New England hospitals that are not and never have been represented in this society. Nevertheless, from time to time, either in medical meetings or in consultation service, or even in friendly association, we come in contact with some members of their staffs or boards of trustees. Should we not use such opportunities to urge the value of good staff organization? Membership in this society carries with it an implication of leadership in surgery. Twenty-seven years ago your first president, Dr. Samuel Jason Mixter, wise and sagacious leader, of whom this memorial gavel is a yearly reminder, said: "Through training of mind and hand, hospital experience under the control of able masters — these are absolute essentials and should be insisted upon in the future as they have not been in the past. It is the duty of this society to use its influence in this direction."

31 Chestnut Street

THE VITAMIN CONTENT OF COMMERCIAL WINTER GOAT'S MILK*

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IT HAS been estimated that the retail value of goat's milk produced in this country exceeds $100,000,000 annually. A large portion of fluid goat's milk is used for infants, for invalids and for consumption in the home of the producer.

Various claims have been made for the superiority of goat's milk over cow's milk. Besley[1] states that of the two, goat's milk has larger amounts of albumin and nonprotein nitrogen, greater quantities of vitamin B_1, a softer curd and smaller fat globules. Richards[2] reports "the fact that goat's milk is alkaline in its reaction while cow's milk is acid, a matter of the greatest importance to persons suffering from hyperacidity of the stomach." According to Gamble, Ellis and Besley,[3] the difference in appearance between the pigmented cow's milk fat and the colorless goat's milk fat appears to be due to a more thorough conversion of carotene to vitamin A in the latter. On the other hand, Potts and Simmons[4] report that analyses of milk carried out at the Bureau of Animal Industry, United States Department of Agriculture, showed no significant differences in calcium, phosphorus, iron and copper content between goat's and cow's milk. Furthermore, a review of the literature revealed relatively little information concerning the vitamin content of goat's milk. Accordingly, more information concerning its quality and vitamin potency is needed for judging its value and use, and this study was undertaken to accumulate such additional data.

EXPERIMENTAL PROCEDURE

The samples of raw goat's milk used in this study were obtained from various localities within an area of about 100 miles from Amherst. Eighteen samples of milk were shipped to the laboratory by the producers in the usual containers, packed in cracked ice. The temperature of the milk on arrival was 32 to 40°F. The samples were examined for fat content and bacteria count within four hours after their arrival. Since the milk had been produced in widely scattered localities, it was impossible to make the vitamin assays immediately following milking, and since information was desired concerning the vitamin content of goat's milk that had been handled under commercial conditions, it was decided to hold the milk in storage for the longest period that might occur under commercial conditions. Accordingly, after the raw milk arrived at the laboratory it was held in a commercial milk-refrigerating room until it was seven days old.

According to the owners the goats were either pure-bred or grade animals. Three breeds were represented, Nubian, Saanen and Toggenburg, the largest proportion of the goats being Toggenburg. They were all normal, healthy animals. Their ages varied for the different herds. The extreme ages were eighteen months and ten years, but the average age was about four years and, judging by the producers' reports, the animals were largely in the latter half of the lactation period. To secure data representative of the Massachusetts industry, samples of goat's milk were obtained from producers having different-sized herds. Furthermore, it will be noted from Table 1 that some samples were taken from a single animal and some were composites from several animals.

All the samples were obtained at the end of April from goats that had received a winter ration of hay and commercial grain mixtures for five or six months previously. None of them had been pastured or had received silage. The quality of the ration obviously varied with the different herds, for the hay was described as "poor quality," "alfalfa," "excellent," "local grown" and "mixed hay," and the commercial grain mixtures were of several brands and of different compositions. In addition, the goats that produced Sample 18 were given carrots and vegetable trimmings as a supplementary noon feeding.

The fat was determined by the Babcock method, and the bacteria count was made by the procedure outlined in *Standard Methods for the Examination of Dairy Products*.[5] A Coleman instrument was used to determine the pH value. The ascorbic acid content of the milk was determined by the method reported by Holmes, Tripp, Woelffer and Satterfield[6] and Tripp, Satterfield and Holmes.[7] The niacin was assayed by the microbiologic method of Krehl, Strong and Elvehjem.[8] The microbiologic procedure of Neal and Strong[9] was used for assaying the pantothenic acid. The riboflavin content was determined by the method reported by Holmes, Jones, Wertz and Kuzmeski,[10] except that potassium permanganate and hydrogen peroxide were used instead of stannous chloride and sodium hyposulfite for discharging any extraneous color. The thiamine content was determined by a modifica-

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tion of the thiochrome method of Hennessy and Cerecedo.[11]

Results

Data concerning the history of the 18 samples and the results of the assays are reported in Table 1, but in order to simplify the discussion of the results they will be considered under separate headings.

Fat

In their studies of goat's milk, Matthews and Weaver[12] found 7.79 per cent of fat and Holm and Webb[13] 6.0 per cent. Gamble, Ellis and Besley[3] conducted a three-year study of goat's milk and obtained an average of 3.50 per cent of fat, with a peak of 5.00 per cent in February, from which time the fat content declined slowly but consistently until December. Lythgoe[14] found that the fat content of 36 herd samples of goat's milk varied from 2.4 to 6.8 per cent, with an average of 4.45 per cent. In assays of 439 samples of individual goat's milk the range was from 1.90 to 9.80 per cent, with an average of 4.43 per cent. Lythgoe also found a peak of 5.13 per cent in February, which was followed by a seasonal decline. In a study of 18 samples of goat's milk, Peterson, Turner and Ralston[15] reported a range of 2.30 to 6.50 per cent, with an average of 4.80 per cent. Besley[1] compared the composition of Holstein milk with combined Toggenburg and Saanen milk and reported 3.50 per cent for the latter. Ormiston and Gaines[16] determined the fat content of milk from eight breeds of goats and found from 4.08 per cent for Toggenburg to 6.37 per cent for Anglo-Nubian, with an average of 4.76 per cent for all breeds, but Trout[17] obtained less — that is, 3.54 per cent for Toggenburg, 4.41 per cent for Nubian, 4.18 per cent for Saanen and 3.84 per cent for the mixed breeds. The variation for his group of 40 samples was from 2.70 to 5.10 per cent, with an average of 3.49 per cent, but in his extensive summary of data reported in the American and foreign literature, he cites a minimum content of 2.29 per cent and a maximum of 7.57 per cent.

In this study the fat content varied from 3.1 to 5.6 per cent and averaged 4.0 per cent. This value is closely similar to the 4.1 per cent reported by Asdell and Marquardt,[18] the 4.09 per cent reported by Turner, Ragsdale and Garrison[19] and the 3.50 per cent reported by Potts and Simmons.[4]

Bacteria Content

A survey of the literature revealed almost no information concerning the bacteria content of goat's milk. Gamble, Ellis and Besley[3] found in 728 samples from 200 to 9800 bacteria per cubic centimeter, with an average of 775. Of these bacteria 87 per cent were *Micrococcus epidermidis*, 11 per cent were *M. aurantiacus*, and 2 per cent were *M. varians*, but none of the bacteria isolated appeared to have pathologic significance.

The bacteria count for the 18 samples of goat's milk under consideration varied from 100 to 6000 per cubic centimeter, with an average of 1300. It will be noted on reference to Table 1 that with the exception of 5 samples the bacteria count was extremely low. The average for 13 samples was 300 per cubic centimeter, a value much lower than that ordinarily obtained for cow's milk.

Hydrogen-Ion Concentration

In his study of the composition of 40 samples of goat's milk, Trout[17] obtained pH values ranging from 6.33 to 6.52. Schultz and Chandler[20] examined 160 samples and found that the hydrogen-ion concentration varied from pH 6.4 to 6.7. The average pH for 86 morning samples was 6.52 and for 74 evening samples 6.54, with an average of 6.53 for the total number. Gamble, Ellis and Besley[3] report that the pH of 4 samples of goat milk ranged from 6.54 to 6.57.

Table 1. *Identification and Vitamin Content of Commercial Winter Goat's Milk.*

Sample No.	No. of Goats	Kind of Bottle		Fat Content	Bacteria Count	Hydrogen Ion Concentration	Ascorbic Acid	Niacin	Pantothenic Acid	Riboflavin	Thiamine
		Size	Material	%	per cc.	pH	mg./l.	mg./l.	mg./l.	mg./l.	mg./l.
1	2	1 pt.	Glass	4.0	6000	6.26	1.4	1.79	3.32	1.38	0.42
2	1	1 pt.	Glass	3.5	100	6.21	0.2	3.24	3.56	2.16	0.49
3	6	1 pt.	Glass	4.1	100	6.35	7.4	2.44	3.52	1.13	0.50
4	3	1 pt.	Glass	3.2	400	6.13	14.7	3.56	5.86	1.31	0.50
5	3	1 pt.	Glass	3.1	5100	6.17	7.4	3.56	4.61	1.10	0.44
6	2	1 pt.	Paper	3.3	400	6.38	8.6	2.67	6.46	1.27	0.46
7	2	1 pt.	Paper	3.3	2500	6.42	7.0	2.61	2.79	1.06	0.42
8	2	1 pt.	Paper	3.4	1200	6.43	9.4	2.72	3.18	1.03	0.44
9	1	1 pt.	Glass	4.9	200	6.27	0.2	—	2.01	1.62	0.46
10	3	1 pt.	Glass	4.6	5200	6.30	10.0	2.80	2.36	1.05	0.50
11	1	1 pt.	Paper	4 4	100	6.32	9.0	3.46	2.81	1.03	0.49
12	1	1 pt.	Paper	4.7	300	6.37	5.2	3.81	3.73	0.92	0.20
13	1	1 pt.	Glass	5.6	800	6.62	7.6	2.93	2.59	1.51	0.50
14	1	1 pt.	Glass	4.7	400	6.59	7.7	2.29	2.57	1.34	—
15	2	1 pt.	Glass	4.0	400	6.55	5.6	—	2.71	1.10	0.47
16	50	1 qt.	Glass	3.6	300	6.43	5.1	3.14	2.52	1.35	0.50
17	50	1 qt.	Paper	3.6	200	6.42	2.0	3.15	3.22	1.27	0.49
18	6	1 pt.	Glass	3.3	300	6.42	7.7	3.23	2.98	0.89	0.44
Averages				4.0	1300	6.37	6.5	2.96	3.38	1.25	0.45

The hydrogen-ion concentration of our samples varied from pH 6.13 for Sample 4 to pH 6.62 for Sample 13, with an average of pH 6.37. This value is somewhat lower than those cited above, possibly because the samples were a week old when examined.

Ascorbic Acid

The biologic method was used in the early study of the vitamin C content of goat's milk. Hunt and Winter[21] fed guinea pigs 20 cc. of cow's and of goat's milk and found a somewhat larger vitamin C activity in the latter. Chakraborty[22] assayed the milk of cows, goats, buffaloes and human beings and found 0.009 mg. of vitamin C per cubic centimeter in goat's milk. Richmond, Grinnells and Satterfield[23] examined 430 samples of goat's milk and found a range of 0.5 to 2.0 mg. per 100 cc. Turner and Garrison[24] assayed 275 samples of morning milk from twenty-five Toggenburg goats within three hours after milking and obtained an average value of 2.0 mg. of ascorbic acid per 100 cc. Gamble, Ellis and Besley,[3] who assayed their samples as promptly as possible after production, obtained a range of 5.0 to 25.0 mg. per liter, with an average of 13 mg., and also observed that the spring and summer milk had more ascorbic acid than did the fall and winter milk. In a comparison of the vitamin C values of cow's, goat's, ass's, mare's and human milk, Cimmino[25] found that goat's milk contained 45 mg. per liter and that dehydroascorbic acid was almost entirely absent. In a study of the ascorbic acid content of Indian foods, Rudra[26] found that goat's milk contained 0.805 mg. per gram. Wildt and Brouwer[27] compared the vitamin C content of goat's and cow's milk during summer feeding on pasture and during stall feeding in winter and found no significant difference. As compared with these values, Frank[28] in guinea-pig assays of human, goat's and cow's milk found that human and goat's milk had practically no antiscorbutic properties. This finding was in accord with that of Meyer and Nassau,[29] who observed the great increase in the number of cases of infantile scurvy in Germany and made a study of the vitamin content of milk, milk powders and milk products. They found that fresh milk from goats fed green fodder was deficient in vitamin C.

The reduced ascorbic acid content of the 18 samples under consideration was extremely variable. Four samples contained almost no ascorbic acid, and the maximum content was 14.7 mg. per liter. The average value for the 18 samples was 6.5 mg. per liter, but if the 4 small and the 1 large samples are eliminated, the average becomes 7.5 mg. for the remaining 13 samples. These values are lower than those for fresh cow's milk, but they could be anticipated since Hand[30] has reported that the reduced ascorbic acid content of cow's milk decreased from 23 to 7 mg. per liter during six days of storage.

Niacin

Apparently investigators have devoted almost no attention to the niacin potency of goat's milk, for the literature consulted contains only one report of such assays. In their study of the vitamin B content of milk from different species of animals, Williams, Cheldelin and Mitchell[31] included 4 samples of mixed milk from Saanen, Nubian and Toggenburg goats. They found from 2.0 to 3.2 mg. of niacin per liter, with an average of 2.5 mg.

The values obtained for the 18 samples of milk under consideration varied from 1.79 to 3.81 mg. of niacin per liter, with an average of 2.96 mg. It is of interest to compare the content of goat's and of cow's milk. Williams, Cheldelin and Mitchell[31] report that goat's milk contains nearly four times as much niacin as does Jersey or Guernsey milk. This relation between goat's and cow's milk is in agreement with that obtained in this laboratory in preliminary experiments.

Pantothenic Acid

A review of the literature concerning goat's milk reveals only one study of its pantothenic acid content. Williams, Cheldelin and Mitchell[31] examined 4 samples of milk produced by Saanen, Nubian and Toggenburg goats. They obtained a minimum of 1.3 mg. per liter, a maximum of 3.2 mg. and an average of 2.4 mg.

The values obtained in this study ranged from 2.01 to 6.48 mg., with an average of 3.38 mg. In view of the paucity of data, it is hardly possible to compare the pantothenic acid content of goat's and of cow's milk, but Williams, Cheldelin and Mitchell report nearly the same value, that is, 2.9 mg. for cow's milk and 2.4 mg. for goat's milk.

Riboflavin

Gamble, Ellis and Besley[3] compared the vitamin G (riboflavin) content of milk from Saanen and Toggenburg goats and from Holstein and Jersey cows by rat-feeding tests at different seasons of the year. They found significant differences favorable to goat's milk. Williams, Cheldelin and Mitchell[31] determined the riboflavin content of milk from Saanen, Nubian and Toggenburg goats. Their values ranged from 0.89 mg. to 1.2 mg. per liter, with an average of 1.1 mg.

The results obtained in this study of the riboflavin potency of goat's milk were extremely variable, ranging from 0.89 to 2.16 mg. per liter, with an average of 1.25 mg. Aside from Sample 2, which contained 2.6 mg. of riboflavin per liter, all the samples contained less riboflavin than was present in cow's milk.[10] The average value for the goat's milk was 1.25 mg., as compared with 1.51 mg. for raw cow's milk. It should be noted, however, that the cow's milk was fresh and the goat's milk was a week old. Moreover, as stated above, the goat ration was limited in variety and contained no grass

silage. On the other hand, Peterson, Haig and Shaw[32] found no decrease in the riboflavin content of cow's milk that had been stored in a refrigerator for seven days.

Thiamine

In their comparison of goat's and cow's milk, Gamble, Ellis and Besley[3] compared the vitamin B_1 potency of milk from Toggenburg and Saanen goats with that of milk from Holstein and Jersey cows. They concluded from the rate of growth of rats that goat's milk, which contained 1 international unit of vitamin B_1 in 4 cc. of winter milk and 3 cc. of summer milk, was richer in vitamin B_1 than was the Holstein and Jersey milk, which contained 1 unit in 6 to 7 cc. of winter milk and 5 cc. of summer milk. In a later paper, Besley[1] reported that combined Toggenburg and Saanen milk had a vitamin B_1 content of 28 international units per 100 gm., as compared with 16 units in Holstein milk. Williams, Cheldelin and Mitchell[31] found in mixed milk from Saanen, Nubian and Toggenburg goats from 0.32 to 0.48 mg. of thiamine per liter, with an average of 0.30 mg.

The thiamine content of the 18 samples of goat's milk used in this study, with the exception of Sample 12, which had a thiamine content of 0.20 mg. per liter, varied from 0.42 to 0.50 mg., with an average of 0.47 mg. This value is significantly higher than that of 0.33 mg. obtained in an earlier study of fresh milk from a herd of Ayrshire, Guernsey, Holstein, Jersey and Shorthorn cows.[10]

Effect of Light

It has been frequently observed that exposure to light affects the stability of ascorbic acid, riboflavin and other vitamins. Consequently, a question may arise concerning the possible effect of light on the vitamin content of our samples of goat's milk during the week that had elapsed before they were assayed. During transit they were protected from the action of light by the packages in which they were shipped. While the samples were in the cold-storage room they were subjected to light of approximately 3-foot candles during the day, that is, eight out of twenty-four hours. Thus it seems probable that light had no significant effect on their vitamin content, even though some were shipped in glass bottles and the remainder in paper bottles. As a matter of record, however, the respective vitamin values of the 12 samples packed in glass bottles and of the 6 samples packed in paper bottles were as follows: ascorbic acid, 5.9 and 7.8 mg.; niacin, 2.92 and 3.09 mg.; pantothenic acid, 3.22 and 3.79 mg.; riboflavin, 1.40 and 1.06 mg.; and thiamine 0.48 and 0.40 mg.

Summary

Eighteen samples of goat's milk were procured from producers located within 100 miles of the laboratory. The samples represented milk produced under routine conditions from normal healthy animals, and were shipped in the usual glass or carton containers, packed in cracked ice. The temperature on arrival was 32 to 40°F. The milk was immediately examined for fat content and bacteria count. The samples were held in a commercial milk refrigerating room until the milk was a week old and then assayed for their vitamin potency.

The average values obtained were as follows: fat, 4.0 per cent; bacteria, 1300 per cubic centimeter; hydrogen-ion concentration, pH 6.37; ascorbic acid, 6.5 mg. per liter; niacin, 2.96 mg. per liter; pantothenic acid, 3.38 mg. per liter; riboflavin, 1.25 per liter; and thiamine, 0.47 mg. per liter.

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MEDICAL PROGRESS

SYPHILIS

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PENICILLIN appears to be capable of playing as dramatic a role in the treatment of syphilis as in numerous other infections, if early indications are correct. This is the outstanding feature of progress in regard to syphilis during the past year. The incidence of this disease has been notably reduced, even without the aid of penicillin — a remarkable feat in time of war.

Public-Health Aspects

In these columns six years ago it was stated that the chance of acquiring syphilis during the average lifetime was approximately 1 in 10.[1] Vonderlehr and Usilton[2] computed this 10 per cent attack rate from figures covering the years 1936 and 1937. The same authors have made a second appraisal covering the years 1939 to 1941.[3] Their data were obtained from the number of persons with early syphilis reporting for the first time at authorized sources of treatment that serve about 5 per cent of the population. The second survey showed that the chance of persons acquiring syphilis by the age of fifty had dropped to 1 in 15, a decrease of one third. This study clearly indicates that during the six-year period 1936–1941 the chance of acquiring syphilis dropped appreciably. These two sets of data should serve as a base line by which the control of syphilis in the future may be judged. The years covered in these surveys are those during which the campaign for the control of syphilis was being intensified. Although the decrease in the attack-rate of syphilis is indeed gratifying, it should be recalled that the United States in 1940 had not yet entered World War II. Turner[4] has reviewed the accomplishments in the control of venereal diseases since 1940. His figures indicate a striking reduction in the level of days lost per man per year because of venereal diseases in the armed forces. In 1940, as many as 1278 days were lost per 1000 men per year, whereas at the time of Turner's writing (1943) the rate was 368 days per 1000 men per year. He credits most of this magnificent accomplishment to the work of venereal-disease control officers who were assigned to camps and to all theaters of operations. This is an example of intelligent utilization of specially qualified medical personnel. Turner believes that a civilian program designed to control venereal diseases should be similarly built around medical specialists in this field. The tasks that lie ahead of the military in respect to venereal diseases are outlined. A public-health step of first importance has been taken by Congress.[5] A new law abolishes all punishment for venereal disease in the armed forces, provided only that the infected person complies with Army or Navy regulations requiring him to report and receive appropriate treatment. Failure to report a venereal infection remains punishable by court-martial or other disciplinary action. This measure recognizes that fear of punishment does not prevent exposure but does promote concealment and self-treatment.

Juvenile Delinquency

Turner[4] also stresses the expansion of educational efforts, particularly those directed to the young women of the community, the maintenance of the gains made against organized prostitution and the problem of the sexually delinquent girl, which is

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not to be confused with prostitution. The last-mentioned source of venereal infection has been becoming distinctly prominent in the last few years. Many authors have referred to it, and some statistics are now available. Among these is an analysis of 4641 contact reports from the Third Service Command.[6] Although reported by soldiers in only three eastern states, this large number of exposures took place with girls in all but nine of the forty-eight states. The pickup to whom no fee was paid was the leading source of infection (64 per cent Whites and 45 per cent Negroes), whereas the paid prostitute constituted only one fifth of the sexual contacts. This emphasizes clearly the important role played by "amateurs." Numerous other publications indicate that the fifteen to twenty age group includes the largest proportionate number of these casual female contacts. Obviously the control of juvenile delinquents is extremely difficult to handle through organized authority. Nevertheless, the public-health literature is replete at this time with reports of ambitious plans from state after state; in many instances they are being carried out with reasonable success. Organized control programs are also under way in many large cities. The juvenile delinquency problem, however, will probably not be solved until an understanding of venereal diseases is brought home to each small community; it can then reach the family unit. Not until that point is attained, will we begin to get at the root of juvenile delinquency. Taft[7] has outlined a seven-point program to attack delinquency, which is based on the same theory. Although he believes that the primary responsibility in meeting the problem lies with the community, it is pointed out that the federal government can do its part. Through the United States Public Health Service three things can be offered in meeting this problem: leadership, funds and trained technical consultants. The duty of the community in rehabilitating delinquents is also portrayed. The value of youth education regarding venereal diseases has been stressed by Bigelow.[8] The teaching of the significant facts about venereal infections in high schools and colleges is strongly advocated. This author thinks that sexual conduct is determined by ethical attitudes and standards more than by knowledge of scientific facts; consequently, an approach through the home, school, church and youth organizations should have its greatest value in developing character and standards of conduct. Nevertheless, scientific information should prevent some infections and should stimulate many persons to seek medical advice promptly when needed. A number of cities and communities have already included plans for youth education in their control programs. The British Board of Education[9] has issued a pamphlet on sex education in schools and youth organizations that is extremely well worked out. One interesting suggestion therein is the appointment of "a really good woman physician, preferably married, youngish, with a modern approach and modern clothes" to handle the problem with girls' organizations. More comprehensive attempts are being made to reach the large Negro population in the southern states. There are also numerous reports from Canada and the Latin American countries, which are encouraging. Puerto Rico is one sadly neglected focus of venereal disease in which an organized campaign is now under way. If these programs can be managed more and more effectively, in conjunction with the admirable programs of the military services, much should be learned that will enable everyone to carry on more efficiently when peace finally arrives. An excellent paper by Ingraham and Greenbaum[10] emphasizes the vital part that can and should be played by the practicing physician who treats syphilis. It is pointed out that with the increase in the amount of venereal disease being privately treated, no control program can succeed without full co-operation of physicians in tracing contacts.

Syphilis in Industry

In the past numerous publications in regard to venereal diseases and industry have been quoted, and the current reports indicate continuation of efforts to work through its various branches. This has been done mainly by approaching the medical departments of large corporations. Unfortunately a relatively small percentage of industrial managements has so far been properly educated. In many plants men are still being discharged or refused work if they have syphilis, regardless of the status of their disease.[11] One report has been uncovered that indicates an approach through the medium of a labor organization.[12] The Executive Board of the California State Federation of Labor has recommended compulsory blood tests for all future members of the union in California. The co-operation of public-health facilities and the California Social Hygiene Association has been obtained. A thorough educational program is being conducted among the entire union membership. In these days of such constant bickering by some labor groups, it is pleasant to find a good word to say in their favor.

Incidence of Syphilis

Statistics for the fiscal year 1943–1944 for all the states, territories, possessions and the Panama Canal Zone are now available.[13] For the United States proper, 100,000 fewer cases of syphilis of all kinds were reported. In only thirteen states was there an increase, and in but four of these was it significant. These figures are compiled from the health officers' monthly statements and do not include the armed forces. Army data indicate that the rate of venereal infection has fallen below preceding peace-

time levels and is less than half that recorded during World War I.[14] If this trend continues, it will be the first war in history during which syphilis has been held in check. This applies to the general public and even more remarkably to the military services.

Experimental Studies

Further studies of *Treponema pallidum* by the electron microscope are available. Mudd, Polevitzky and Anderson[15] have compared several strains with other spirochetes and confirmed the findings of previous students. Cares[16] has reported on the differential motility characteristics of *T. pallidum*. His material was obtained from infectious lesions rather than from cultures. Three other forms of spirochetes were encountered. The identifying motility types of locomotion and changes in shape are carefully described. Although this work was done with the use of the electron microscope, a good deal of the motility of *T. pallidum* can be observed with an ordinary microscope. A review of this article should be beneficial to any practitioner capable of and equipped to do dark-field examinations.

An interesting study has been reported regarding the effect of fever on the distribution of arsenic in the tissues of rabbits injected intravenously with Mapharsen.[17] It was found that there were distinctly higher concentrations of arsenic in the tissues of rabbits treated with Mapharsen and fever than when the former was given alone. Observations made twenty-four hours after treatment revealed that significant amounts of arsenic were still present in all the tissues in the fever-treated group; whereas in the group receiving Mapharsen without fever only negligible amounts of arsenic could be detected in tissues other than the kidneys and lungs. These findings suggest that fever may either bring about an increased deposition of the drug in the tissues or fix it more firmly, thus delaying elimination. Both factors may of course be involved. These observations may explain the enhanced therapeutic action of arsenical drugs when combined with fever, and perhaps also the increase in toxic reactions.

Many reports have appeared in recent years regarding the use of ascorbic acid as a detoxifying agent during treatment with intravenous arsenical compounds. During the last year several publications have appeared on detoxication by means of *p*-aminobenzoic acid. Sandground[18,19] carried out extensive experiments with rats. Massive acutely poisonous doses of several pentavalent arsenical drugs were used. The survival rate among rats that received *p*-aminobenzoic as compared with that of controls was so high that its protective role seemed established beyond question. Furthermore, there appeared to be no inhibition of the trypanocidal action of the arsenic. Subsequently, Sandground and Hamilton[20] carried out parallel experiments with lethal doses of neoarsphenamine and found the protective capacity of *p*-aminobenzoic acid equally effective. The clinical implications of these findings, especially with respect to the intensive treatment of syphilis, seemed promising, but when this work was applied clinically, the results were discouraging.[21] A small group of patients with neurosyphilis were given *p*-aminobenzoic acid in conjunction with pentavalent arsenical compounds. Such oral administration, however, did not prevent nitritoid crises, gastrointestinal reactions or optic-nerve damage. This apparent failure may not be as disheartening as it sounds, and one can still hope for more satisfactory results with further work. Another group of investigators,[22] studying the detoxifying actions of several organic acids, confirmed Sandground's findings in experiments on animals. It was further observed that the effect is most favorable when the arsenical and the protective agent are injected intravenously in the same solution.

Pathology

Although comparatively little medical literature has been available from Germany in recent years, one quite interesting report has turned up. Gottschalk[23] quoted the Magdeburg combined morbidity statistics for the period 1928–1936 regarding venereal diseases as a cause of death. These statistics include 8182 deaths for which both the clinically determined cause of death and autopsy findings were available. Of this number 322 (3.9 per cent) died of disease that was clinically diagnosed as syphilis, and in 214 of these (66 per cent) the clinical diagnosis was confirmed by autopsy findings. Another 192 cases were found in which the autopsy determined syphilis to be the cause of death, bringing the total number to 406 cases of death due to syphilis. By means of autopsy, therefore, 26 per cent more cases were diagnosed in which death was due to syphilis than by clinical findings alone. Aneurysm and tabes dorsalis were the two syphilitic conditions most frequently incorrectly diagnosed clinically. Black-Schaffer and Rosahn[24] report a continuation of their study of autopsy reports from Yale University School of Medicine. An attempt was made to correlate the serologic tests for syphilis in 313 autopsies on syphilitic patients. Serologic positivity was significantly more frequently associated with anatomic lesions of syphilis than was serologic negativity. Analysis of the data from numerous standpoints suggested that increasing activity of the disease is associated with an increasing frequency of positive blood tests. The likelihood of syphilis being the primary cause of death was more than twice as great in patients with positive serologic tests than in syphilitics with negative tests. These findings are quite interesting in view of a strong tendency among syphilologists to disregard the so-called "serofast status," which not infrequently persists in late syphilis even after what is

considered adequate therapy. It poses the question whether the correct definition of adequate therapy is actually known.

Six cases of acute encephalopathy were encountered by Young and Gordon.[25] These patients were being treated with a heavy-dosage, multiple-syringe, intensive schedule. All received the conventional therapy for hemorrhagic encephalitis, but only one patient recovered. The clinical pictures and autopsy reports are given. Typical necropsy findings were edema and numerous petechial hemorrhages of the entire brain, slightly larger hemorrhages in the pituitary gland, cloudy swelling of the liver and congestion of the kidneys and alimentary canal. This particular reference is quoted to emphasize one of the grave disasters that may be encountered in massive-treatment programs. A distressingly high percentage of all types of treatment reactions is still being observed, even with the modified intensive schedules that are in general use in military stations, governmental treatment centers and many large civilian hospitals. All this work must still be considered experimental, as has been repeatedly emphasized in the past. Any physician treating syphilis is frequently besieged by his more alert patients with inquiries about, or demands for, rapid treatment. It is unfortunate that the lay press is so prone to publicize experimental medicine.

Diagnosis

Serologic Tests

In an editorial, "The Serology Was Positive," Moore[26] makes a plea for a correct usage of terminology. He points out that "serology" is a branch of science and not a test. It is a term that cannot be limited to diagnostic tests for syphilis, nor can serology be expressed as "positive" or "negative." It is pointed out that the correct expression is "the serologic test was positive." Moore goes on to call attention to the fact that the adjective "serologic" is not applicable to spinal fluid tests, as this fluid is not a serum. It may be added that a commonly accepted abbreviation for the term "serologic tests for syphilis" is "STS." This will be seen in much of the literature pertaining to syphilis at the present time. It is always correct, in addition, to name the actual test employed, if one so desires.

For several years the Kahn verification test has been employed in some laboratories in an attempt to detect false positive tests in routine serologic practice. Kahn[27] has continued his work with this special test and has introduced improvements. He has determined differential characteristics of specific and nonspecific serologic reactions with different temperature and electrolyte requirements. These procedures "type" serodiagnostic reactions on the basis of their specificity. The verification test may thus be applied to seropositive cases that are free from clinical indications of syphilis. If nonspecific type reactions are found in the absence of any history or clinical evidence of syphilis, Kahn believes that the positive reactions are nonspecific and syphilis can be ruled out. This is certainly a step in the right direction. If this work is corroborated, and if the verification test becomes widely available, it should be of considerable value.

An English Navy innovation has been reported by Crick,[28] who recommends the use of serologic precipitation tests for syphilis aboard large ships in wartime. This procedure has proved of value in dark-field-negative lesions and suspicious eruptions. It has also relieved the hospital ships in routine blood examinations. It is not advocated to the exclusion of hospital laboratory tests, but is recommended as an adjunct in certain circumstances.

False Positive Tests

An analysis has been made by Kolmer[29] of the results of nine serologic surveys from 1935 through 1941. A large number of the false positive reactions in the serodiagnosis of syphilis were found to have been due to errors in the collection of blood, resulting in excessive contamination or hemolysis, and to faulty laboratory technic. Technical errors inherent in the tests themselves may give false indications even in skilled hands. Comparing the results of these various serologic surveys with another in 1943, Kolmer found an appreciable decrease in the percentage of false positive reactions in serums of normal nonsyphilitic individuals. The author classifies the diseases and conditions known or suspected of causing biologic false doubtful and positive reactions into three groups. First, a variable incidence is seen in yaws, pinta, leprosy, malaria, vaccinia and vaccinoid, infectious mononucleosis and virus pneumonia. A second group of ten febrile diseases is stated to show an unknown incidence. A still larger third group of conditions is mentioned in which the evidence regarding false positive tests is not conclusive. A listing of these two latter groups will be omitted to avoid confusion; it is suggested that suspected false positive reactions occurring in diseases other than Kolmer's first group be subjected to exacting scrutiny. In Kolmer's paper it is stressed that the entire responsibility of the diagnosis of syphilis should not be placed on the laboratory findings and that there is no substitute for thorough clinical examination. In cases in which the reactions are persistently positive it is frequently advisable to make a tentative diagnosis of syphilis and institute treatment. This is particularly true if the positive reports come from more than one laboratory and by multiple technics. A situation such as pregnancy is an additional indication for treatment.

It seems apropos at this point to enumerate a few suggestions for the prevention of hemolysis of blood specimens. The syringe and needle used to draw blood should be dry and sterile. Alkalies and other

chemicals should be avoided if syringes are boiled. Blood should never be sprayed through the needle into the tube; the needle should be detached, and the blood should be expelled slowly against the side-wall of the tube. The tube should be placed in a cold place at once, preferably in a refrigerator, especially in warm weather, and should be kept there until mailed. These procedures will help to reduce the number of anticomplementary specimens.

In previous progress reports, references to false positive tests after smallpox vaccination have been quoted. Further confirmation of this observation has been published by Favorite.[30] A group of 202 medical students and nurses known to have negative serologic tests were vaccinated and repeatedly tested, using three technics. Twenty-four persons (11.8 per cent) were seropositive at some time following the vaccination. These cases were retested every two weeks. There was a gradual diminution of reactions, with all becoming negative by the end of one hundred and twenty days.

A group of investigators at the Iowa State Laboratory[31] studied the reactions in the serums of 993 known syphilitic persons by three technics. It was found that 13.5 per cent gave entirely negative reactions for all three tests and that 9.7 per cent gave contradictory reactions. It is a frequent observation that these contradictory reactions may persist or may disappear, with or without antisyphilitic treatment. These authors offered several explanations for the disappearance of contradictory reactions. It is stated that they may be due to the development of a latent nonreacting stage of the disease, to a spontaneous cure or to causes other than syphilis that cease to exist. The authors think that the last explanation is the most probable and cite a number of cases to substantiate their belief. This spontaneous reversal to a negative state may require a period of weeks or months. It is again stressed that physicians should not base their diagnoses solely on serologic reports.

The responsibility of ruling out syphilis is equal in importance to that of diagnosing it. Taussig[32] reports in this vein and quotes illustrative cases. He offers a list of suggestions to avoid errors in diagnosis in patients who show no other evidence of syphilis than a repeatedly positive serologic test. One point to bear in mind is the fact that serums positive with less sensitive technics, such as the standard Wassermann test, but negative with highly sensitive tests are probably not syphilitic. An instance of false positive serologic tests for syphilis in several members of a family has been reported.[33]

It is quite universally accepted that cerebrospinal fluids are much less likely to yield false positive reactions. This may indicate that the reagin-like substances that are thought to occur in the blood serums of nonsyphilitic persons yielding false positive reactions do not occur in cerebrospinal fluids. An article has appeared, however, reporting 8 cases with false positive spinal-fluid Wassermann reactions.[34] Seven of these occurred during the course of meningitis. In 5 cases two different organisms were cultured from the spinal fluid; 2 were aseptic. In 7 of the cases the blood was seronegative.

Clinical Problems

Early Syphilis

An interesting study of 2451 newly inducted soldiers revealed a surprising amount of syphilis.[35] All had been classified 1-*A* by an induction board and were presumably free of venereal disease. Fifty-five men were found to be definitely syphilitic: 4 had early syphilis; 8, neurosyphilis; and 43, latent syphilis. An additional 61 men were thought to have had previous syphilitic infection and to have been cured by treatment. Only the 4 men with early infection showed physical evidence of the disease, and only 10 of the others had a doubtful or positive serologic test. This indicates the importance of an adequate history in conjunction with serologic testing and physical examination. A good discussion of the principles of diagnosis in syphilis and the comparative merits of available procedures has been given by Barnett.[36] The importance of meticulous examination is stressed. The ease with which minor bits of clinical evidence may be overlooked is well illustrated.

As in many other diseases, the failure to make a diagnosis of syphilis may often be due simply to not thinking of its possibility. Bearing the disease in mind is of utmost importance with early lesions in the seronegative stage. An interesting commentary on this point has been published by Spatz.[37] This author reports a series of 11 consecutive cases of primary syphilis in which only 3 presented the classic type of painless, hard, solitary chancre. The lesions in the remaining cases resembled the ordinary chancroidal or balanitic ulcerations; they were not indurated, often were multiple and sometimes were painful. All these cases were diagnosed by dark-field examination. The question is brought up how many latent or advanced cases of syphilis were not detected in their early stages simply because the primary lesions were so atypical or minor as not even to suggest syphilis to the examiner. Each and every case with a genital ulcer of any description should be subjected to dark-field examination. This applies likewise to many lip and mouth lesions.

The misleading appearance of a meatal chancre has been stressed by McCarthy.[38] It often suggests a mild or recurrent gonorrhea. In the earliest stages it may even appear to be an abortive herpes genitalis. Induration eventually becomes evident, however, and is a sign of utmost diagnostic importance. If the possibility that the lesion is syphilitic is recognized, the problem should be simple. Intraurethral chancres occurred in 8 (11 per cent) of 70 patients with

penile lesions observed by Loveman and Morrow.[39] The urethral discharge in these cases should be serosanguineous or seromucoid, as contrasted to the thick purulent discharge seen in gonorrhea. Mild symptoms of obstruction to the flow of urine may be present. Here again, painless indurated nodules should be palpable. Dark-field examination from the discharge or from the regional lymph nodes should be positive.

Lymph-Node Puncture

Loveman and Morrow,[40] have also stressed the value of dark-field examination of lymph nodes in the diagnosis of early syphilis. Twenty-three of 25 cases of early syphilis yielded positive findings by this method. In 12 (60 per cent) of 20 cases dark-field examination from the local lesions resulted in negative findings. A general discussion of technic is given. Agee[41] writes in a similar vein and points out the value of lymph-node puncture in patients whose satellite nodes persist after the healing of the primary lesion. He has found positive dark-field examinations after as much as eight weeks' intensive therapy. This might arouse speculation regarding the value of one of the commonly used criteria of the effectiveness of early treatment. The rapidity with which surface lesions become dark-field negative under various forms of treatment is stressed as an indication of the effectiveness of therapy. Agee's article indicates that viable organisms may be found in lymph nodes after many weeks of intensive treatment. This should stimulate more thought and conservatism in acclaiming the value of intensive therapy. Twenty years from now we may be disappointed in present-day methods, including the magic of penicillin. There may be more value than we realize in prolonged courses of treatment for syphilis.

Bone Syphilis

Francis and Kampmeier[42] have reported an interesting study of bone lesions found in late acquired syphilis. Roentgenographic evidence of the disease was found in one hundred and seventeen bones in a series of 67 patients. The order of frequency of the most usual sites of bone involvement was as follows: tibia (29 per cent), clavicle, skull, fibula and femur. Lesions were found in twenty different bones. The pathologic findings of tertiary syphilis of the bone are described. In the series reported, periostitis, gummatous osteitis and sclerosing osteitis were found. The amount of bone syphilis reported by these men is much greater than is commonly observed. It must be remembered, however, that they were seeking this one feature by routine x-ray studies rather than by clinical means.

Syphilis of Stomach

Although syphilis seldom produces gastric lesions, it is a diagnosis that may be easily missed. Cunha[43] has recently published his observations on this topic. He believes that a positive serologic test in a patient with gastric deformity demonstrated by x-ray calls for an immediate re-evaluation of the gastric diagnosis. It is pointed out that there is no reason why a syphilitic patient cannot have a malignant neoplasm and that a benign ulcer can also occur in a syphilitic person. Diagnostic features that point toward syphilis of the stomach are outlined as follows: an unduly long history of illness, comparatively mild anemia, higher free-acid values than usual, the absence of gross and occult blood, and extensive tissue involvement as seen by x-ray. Cunha has observed 9 cases of syphilis of the stomach.

Syphilis of Liver

An excellent study of syphilis of the liver has been reported by Hahn.[44] His data on 1165 adult syphilitic patients were obtained from autopsy material at the Johns Hopkins Hospital over a period of nearly thirty years. He found no autopsy report of early syphilis of the liver. The incidence of late syphilis of the liver among the syphilitic patients was 4.9 per cent. The most outstanding pathological finding was the focal gummatous nature of late hepatic syphilis. An analysis of the clinical findings, verified by pathological reports, revealed that no single manifestation was constantly or even usually present. Abdominal pain seemed to be the most significant subjective complaint. The most frequent physical finding was a palpable liver. The spleen was also palpable in many cases. The blood was seropositive in 81 per cent of the patients. Not one patient with late syphilis of the liver had received adequate therapy for early syphilis. The median estimated duration of syphilis was fifteen years. The correct hepatic diagnosis had been suggested in only 12 per cent of the total. Portal cirrhosis and carcinoma of the liver accounted for over 50 per cent of the erroneous diagnoses. It was found that hepatic syphilis rarely produces ascites, huge livers, pronounced weight loss, high septic fever or severe toxemia. There was no evidence that liver damage due to syphilis predisposed to hepatic injury from arsenicals. Portal cirrhosis rarely occurred in association with definite hepatic syphilis. This is a thorough study that merits careful scrutiny by internists as well as physicians in general practice, even if they have no interest in or do not treat syphilis.

Cardiovascular Syphilis

More publications than usual have appeared on the various phases of this topic during the past year. Many are of general interest, whereas others seem to be of value mainly to cardiologists, who deal with the obtuse facets of cardiovascular disease.

Mattman and Moore[45] point out that, although uncomplicated syphilitic aortitis is often an asympto-

matic disease, the extent to which this is true varies not only with the skill and diligence of the clinician but also with the extent of pathologic damage to the aorta. These authors compare two groups of patients observed at the Johns Hopkins Hospital. In a series of 105 patients found at necropsy to have uncomplicated syphilitic aortitis, the clinical diagnosis had been correctly made or suspected before death in only 41 per cent. The authors then add an additional series of 79 patients, observed ten years later, in which the incidence of correct clinical diagnoses had increased to 68 per cent. This appears to indicate that Moore's criteria for the clinical diagnosis of uncomplicated syphilitic aortitis are valid. A keener appreciation of them will, of course, increase the percentage of accurate diagnoses. Hypertension, extensive arteriosclerosis and rheumatic heart disease must, if possible, be ruled out. Moore emphasizes the following symptoms and signs in the diagnosis of syphilitic aortitis: roentgenologic demonstration of dilatation of the first portion of the aorta; heart failure or lowered cardiac reserve in the absence of other causes; localized substernal pain (to be differentiated from anginal pain); and characteristic changes in the aortic second sound. Dressler and Silverman[46] write in a similar vein on the same topic. The interesting feature of their report is the finding of syphilitic aortitis in 8 of 50 cases of congenital syphilis. It is their belief that this condition is more frequent in congenital syphilis than has heretofore been held.

Jones and Bedford[47] describe a series of 103 syphilitic patients subject to paroxysmal pain in the chest that was investigated with special regard to its clinical characteristics. The average period between infection and the onset of pain was twenty-four years. The clinical findings included varying degrees of dilatation of the aorta, cardiac enlargement, aortic incompetence and essential hypertension. Seventy-six patients suffered angina on effort, and 64 had pain apart from effort. Nocturnal attacks were of common occurrence and were usually independent of paroxysmal dyspnea. Symptoms of coronary thrombosis not attributed to syphilis occurred in 10 cases. Post-mortem findings are reported on 12 cases. Pathologic evidence that uncomplicated aortitis causes anginal pain was lacking. Stenosis or occlusion of the coronary ostia was usually found in conjunction with typical syphilitic lesions, but it is stated that atheromatous and thrombotic coronary occlusion may be coincident with syphilis of the aorta. These authors do not believe that an atypical or pseudoanginal syndrome due to syphilitic aortitis exists.

It is stated by Arkin[48] that syphilis is responsible for about 20 per cent of the cases of chronic cardiac disease in adults. This author stresses the preventable nature of syphilitic heart disease, and estimates that early diagnosis and adequate treatment should prevent at least 90 per cent of cases of cardiovascular syphilis. He stresses the need for a periodic physical examination and roentgenographic study of every patient with evidence of syphilis. Arkin's criteria for the diagnosis of uncomplicated aortitis are slightly more elaborate than those of Mattman and Moore.[45] Aortic insufficiency is discussed at some length by Hammon.[49] Syphilitic aortic insufficiency is one of the eight groups into which this author divides these cases. He points out that repeatedly negative serologic reactions occur in from 10 to 15 per cent of cases of syphilitic aortitis. The clinical diagnosis is elaborated in some detail, and the author describes several interesting cases in which syphilis was a factor of the incorrect diagnosis.

Jones and Bedford[47] found abnormal cardiograms in 57 of 94 syphilitic patients subject to paroxysmal pain in the chest. Cole and Bohning[50] paid special attention to electrocardiographic patterns in cardiovascular syphilis. They have correlated the post-mortem findings and electrocardiograms in 30 cases. No specific pattern was found to be pathognomonic of syphilitic cardiovascular disease, but there were 11 cases of left ventricular preponderance and 3 cases with an anterior-wall infarction pattern. These seemed frequently due in whole or in part to syphilis. Parsonnet and Bernstein[51] wrote on the same topic. They consider the electrocardiogram of vital importance as a diagnostic, prognostic and therapeutic guide in cardiovascular syphilis, but state that a diagnosis cannot be made from it alone. They also point out that some of the methods of treatment are factors in initiating cardiographic changes that are indicative of myocardial damage.

Neurosyphilis

O'Leary and his associates[52] have published an excellent analysis of the spinal-fluid findings in asymptomatic neurosyphilis. A general classification of spinal fluids is given in tabular form, according to the degree of abnormality observed in each of the five usual tests. Thus the character of the impending nervous-system involvement may be anticipated and the progress of the disease and the effect of treatment may be properly estimated. It is stated that if the spinal fluid is still negative by the fourth year of the disease, neurosyphilis will probably not develop.

Although acute syphilitic meningitis is a comparatively uncommon complication of syphilis, 15 cases are reported by Skogland.[53] It is pointed out that acute meningitis usually occurs in early syphilis and in untreated or inadequately treated patients. The author states that the blood Wassermann reaction is negative in approximately a third of the cases. Three clinical pictures may be seen: acute hydrocephalus, acute meningitis of the vertex and acute basilar meningitis. Recovery is usually prompt with proper treatment, trivalent arsenic being the initial choice, but sequelae may occur. The author's cases illustrated the three different

types. Aring[54] has also written on acute syphilitic meningitis. He is in general agreement with the preceding author and stresses the importance of intensive therapy. It is pointed out that tryparsamide or fever therapy may be required in some cases.

Syphilis of the spinal cord is discussed at considerable length by Adams and Merritt.[55] These authors classify and discuss spinal syphilis based on pathologic changes. They point out that a pure form of spinal syphilis without lesions of the brain is exceptional, and state that the basic pathologic lesion is probably chronic inflammation of the spinal meninges. Almost every conceivable cord disease may be simulated clinically by spinal syphilis. The authors believe that the introduction of any foreign substance intrathecally, whether a spinal anesthetic or arsphenamized serum, in a patient who has neurosyphilis is dangerous. The clinical results in the treatment of spinal neurosyphilis are discouraging.

The Medical Corps of the Army has set up a special program for the management of neurosyphilis.[56] Certain general hospitals are designated as treatment centers, and all cases diagnosed as neurosyphilis are transferred there for diagnostic review and treatment. It is expected that the bulk of cases will be asymptomatic, with minor spinal-fluid changes, will respond relatively quickly to therapy and will be retained in military service. All other cases will be separated from the service after optimum treatment. Thereafter the United States Public Health Service will maintain observation and treatment as indicated.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**
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CASE 31031

PRESENTATION OF CASE

A twenty-nine-year-old woman was admitted to the hospital complaining of a chronic productive cough and abdominal pain.

Twelve years prior to admission the patient began to suffer with chronic cough. This was often accompanied with fever and was productive at times of as much as a cupful of mucopurulent, foul-smelling sputum a day. The sputum was never blood streaked until a year before entry, when flecks of blood were first noted. The cough and streaking became increasingly severe and were associated with vomiting, often at the end of a paroxysm. On several occasions she vomited intractably for several days at a time. On two occasions she was said to have vomited blood, although at no time did the vomitus have a coffee-grounds appearance. About six months prior to entry a bronchoscopy and lipiodol study were performed, following which she felt better for a few weeks. The blood streaking of the sputum increased, however, until it occurred daily and was most marked in the morning. About three weeks prior to admission she became so exhausted that she was forced to remain in bed; the slightest exertion often induced a severe paroxysm of coughing followed by vomiting. She was able to retain little food, and the tongue and mouth became sore. She had lost about 16 pounds during the year before entry. Five days before admission she developed severe pain under the costal margin in the right upper quadrant, radiating to the epigastrium but not to the back. The pain occurred intermittently in attacks lasting up to twelve hours. There was no diarrhea, constipation, abnormal stools or jaundice. She was admitted to the hospital for study.

The patient had been married for three years but had been unable to become pregnant. She had been a heavy smoker but had cut down considerably in the few months prior to admission.

Physical examination revealed a well-developed and well-nourished woman who did not appear particularly ill. The tongue was beefy red and moderately smooth. The mouth contained numerous small ulcers on the mucous membranes. The lungs revealed only a few medium moist rales at the bases. The heart was negative. There were considerable tenderness and muscle spasm in the right upper quadrant. A tender mass, believed to be the liver, was palpable in this area, extending down almost to the level of the umbilicus; no definite edge could be felt. The spleen was not palpable. There was a lack of precise differentiation between sharp and dull sensations in the lower legs, and some questionable loss of position sense. Vibration sense was diminished in the left lower leg. The deep tendon reflexes were present but the ankle jerks were weak. The plantar responses were not elicited.

The temperature was 99.4°F., the pulse 100, and the respirations 24. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood showed a white-cell count of 11,200, with 93 per cent neutrophils, 4 per cent monocytes and 3 per cent eosinophils. The hemoglobin was 11.8 gm. The urine had a specific gravity of 1.028, with a ++ test for albumin; the sediment contained a few red cells, 15 white cells and a rare granular cast per high-power field. The stools were brown, and a guaiac test was negative. The serum nonprotein nitrogen was 23 mg. per 100 cc., the sugar 78 mg., the protein 6.4 gm. and the chloride 94 milliequiv. per liter. The van den Bergh reaction was normal. The prothrombin time was 24 seconds (normal, 18 to 20 seconds). A bromsulfalein test showed 40 per cent retention of dye in forty-five minutes.

A roentgenogram of the chest was within normal limits. A gastrointestinal series revealed displacement of the stomach to the left and downward displacement of the hepatic flexure of the colon, but was otherwise negative. The lower border of the liver was not well demonstrated. An intravenous pyelogram revealed only a low right kidney. A Graham test was negative.

The patient was given numerous infusions of dextrose in saline together with vitamin B complex, haliver-oil capsules and hykinone. The white-cell count rose to 25,600, with 79 per cent neutrophils, 11 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophils.

On the nineteenth hospital day a laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. J. H. MEANS: "About six months prior to entry a bronchoscopy and lipiodol study were performed, following which she felt better for a few weeks." Are you holding back what was found?

DR. BENJAMIN CASTLEMAN: That is all that is in the record.

DR. CHESTER M. JONES: It was done elsewhere.

DR. MEANS: Apparently no Hinton test was done but I do not believe that the patient had syphilis.

*On leave of absence.

Dr. Holmes has just arrived and I need him. Since time is short, I shall put it up to him this way. If you glance at the first paragraph in the abstract you will see that for twelve years this woman was apparently coughing up purulent sputum, which for a year had often been bloody. She raised as much as a cupful; it smelled bad but later it states that x-ray examination was negative.

Dr. George W. Holmes: That is correct.

Dr. Means: I have a case of tuberculosis in mind in which the x-ray films were reported to be negative for tuberculosis.

Dr. Holmes: That is unusual. About the only time when x-ray films are negative in pulmonary tuberculosis is when the lesion is in the bronchus. You can have an ulcerating lesion in the bronchus with tubercle bacilli in the sputum and a negative x-ray film. You cannot have parenchymal tuberculosis and a negative x-ray film.

Dr. Means: One of the wisest men on diseases of the chest, under whom I was fortunate enough to be a student, was the late Dr. Frederick T. Lord. He said that any patient who had a story of this sort must have a chronic bronchopulmonary suppurative process of some kind. If not in the lung, at least in the bronchus.

Dr. Holmes: Do not let me mislead you. The fact that the x-ray films are negative does not prove that the patient did not have a lesion in the bronchus.

Dr. Means: I know that very well. The answer is that the radiologist cannot necessarily determine a lesion of the bronchus.

According to Dr. Lord's philosophy, if I remember it correctly, this woman ought to have a chronic lung abscess or bronchiectasis. It is too long a history for abscess, however. A lung abscess would have cleared up or would have killed her by that time; therefore it must be bronchiectasis. Dr. Holmes could not demonstrate bronchiectasis, I suppose, if the cavities were empty. Is that correct?

Dr. Holmes: We miss a certain number of cases but this woman's chest is entirely normal. I hardly think that she could have had bronchiectasis.

Dr. Means: How could she have raised a cupful of foul-smelling sputum daily for twelve years and not have had anything in the chest? Had she a fistulous tract that fed pus into the bronchus from somewhere else?

Dr. Holmes: We do not know whether the observation was accurate. The material may have come from the stomach.

Dr. Means: The gastrointestinal tract was reported negative by x-ray study.

Dr. Holmes: The x-ray films do show a large liver.

Dr. Means: I am going to get to that. Let us stick to the thorax for the moment. I was thinking about the esophagus and the bronchus. Are they mixed up with one another or connected in some unholy alliance?

Dr. Holmes: If they are, we have no evidence of it.

Dr. Means: She was said to have vomited blood and, unless it is a perfectly erroneous history, I am forced to conclude, x-ray or no x-ray, that she either had or had had some sort of chronic bronchopulmonary suppurative process. I do not believe that these facts fit with any other interpretation, and a little thing like a negative x-ray should not shake one in one's argument if one thinks that the premises are sound. We are told that she was vomiting. If this was all gastrointestinal in origin it seems to me that Dr. Holmes ought to see something in the gastrointestinal tract beyond a little pushing of the liver in a southeasterly direction. What can you tell about the gastrointestinal tract, Dr. Holmes? Is there anything else besides the pushing down of the liver?

Dr. Holmes: I did this examination myself and that is all I could or can see.

Dr. Means: But you are willing to say that the liver is big.

Dr. Holmes: Yes.

Dr. Means: There have been cases in which the radiologist has said that the liver was big and the clinician has said that it was not big, and Dr. Castleman has found that sometimes the radiologist was right and sometimes the clinician was right. But here both the clinician and the radiologist thought that the liver was big; ergo, I shall say that the liver was big. Of course if the patient had a chronic bronchopulmonary suppurative process with a big liver she is entitled to have had amyloid disease, but I do not think that amyloidosis would explain the acute picture of severe pain in the right upper quadrant.

I have said all I need to say about the lung situation. I do not believe that it was tuberculosis.

In these exercises we usually try to explain the whole picture on the basis of a single underlying disease. We are taught that that is the right thing to do in differential diagnosis. If you stick too rigidly to it, however, you come a "cropper" a certain number of times, because a person can have two diseases. Whether the five-day story of abdominal pain has anything to do with the thoracic story, I do not know. I suppose we should try to relate it, but it does not have to be related. One thing is evident. I am sure that she had an avitaminosis, which explains the stomatitis, the raw red tongue, the sensory changes, the reflex changes and so forth. The clinicians gave her high-powered vitamin therapy, so evidently they thought the same.

On physical examination we are told that this woman was well nourished, although she had lost weight. She might have been overweight to start with. I do not know why she did not look sick. She was said to be exhausted and was forced to stay in bed. Sometimes neurotics take to bed, but she was not neurotic I should say. I do not know

whether she had syphilis. There is no reason to suppose that she did. I do not believe that she had tuberculosis of the liver, but she did have a big liver. I once met my Waterloo at a clinicopathological conference in St. Louis because I had a case of big liver and jaundice and asked Dr. Chester M. Jones before I got on the train if I should consider hepatic tuberculosis. He said, "No; it is so rare that you can forget it." But it was tuberculosis of the liver.

A word or two about the acute attack. I tried to think of the various possible causes. One should always think of lymphoma, but I do not believe that lymphoma could have explained the picture.

I should like to have more than one body temperature. Was it a septic chart?

DR. CASTLEMAN: No; it was flat, the temperature reaching 99.2°F. on only one occasion.

DR. MEANS: This is really difficult — an infectious process without any fever to speak of. I still do not believe that it was cancer. Cancer of what? Of the liver, I suppose. She could not have had cancer of the lung for twelve years, that is sure. Dr. Holmes could find nothing in the lung. If the acute attack was related to the process in the lung, it must have been a process in the lung that was infectious, such as a bronchiectasis. I looked up in some textbooks to see if there was any kind of suppurative process in the lung that gives rise to suppuration in the liver. I tried to find whether a suppurative bronchopulmonary disease may extend through the diaphragm and cause diaphragmatic abscess, thus dislocating the liver. We are told that it was a big displaced liver. I could not, however, find a word about that in my brief literary studies, so perhaps we cannot connect the two processes.

How about a blood-borne infection from the lung? Could a blood-borne infection get from the lung to the liver? It could through the hepatic artery, I suppose, but it seems extremely unlikely.

Let us see what we can get from the laboratory work? There were no lymphocytes in the first smear. I asked Dr. Wyman Richardson what that meant and he said that it made no sense to him; he added that it probably was a poor smear and that the examiner had counted only 100 cells. He is probably right, so that I am not going any farther with that. He also said that scarcity of lymphocytes was in favor of infection, but 3 per cent of eosinophils was against it. So there we are. They found some lymphocytes the next time though. The white-cell count was 25,000. This favors an infectious process. The nonprotein nitrogen, sugar and protein levels and the van den Bergh reaction were normal. The chloride was slightly down. The prothrombin time was only slightly elevated, but there was a positive bromsulfalein test. Would you call it an impressive dye retention, Dr. Jones?

DR. JONES: Forty per cent — yes.

DR. MEANS: So I am forced to believe that the liver was sick at least. She had a big sick liver. What kind? Infectious, I think. How much hepatitis can one have without jaundice?

DR. JONES: A great deal.

DR. MEANS: She could have had acute cholecystitis, I suppose. That would fit this five-day story of severe pain at the right costal margin, radiating to the epigastrium but not to the back. It does not have to go into the back. One can have gall-bladder pain intermittently for twelve hours. That part of the story is all right, but with a big sick liver we must infer more than gall-bladder disease. Also, the Graham test was negative.

I thought of multiple liver abscesses in some way due to the old infection. I could not find any literary support for that hypothesis or for subdiaphragmatic abscess; but certainly there must have been something acute going on in the region of the liver, because of the acute onset of pain, the mounting white-cell count and the tenderness and spasm over the liver. I am much impressed by the last point.

That is the best that I can do. I mentioned a number of possibilities, some of which I am sure were not present. I believe that she had a chronic bronchiectasis. I believe that all the vomiting in the absence of any positive findings in the gastrointestinal tract ought to be interpreted as the result of terrific coughing. At any rate there is no positive evidence of gastrointestinal disease that permits a diagnosis, so that I shall stick to the facts and say that she had a chronic bronchopulmonary process, probably bronchiectasis of long standing. Did she have clubbed fingers?

DR. CASTLEMAN: No.

DR. MEANS: I do not believe that she had cancer, tuberculosis, actinomycosis or lymphoma. I mentioned the possibility of an amyloid liver, but that does not explain the full picture. I am therefore forced to say that she had some kind of infectious process of the liver. Where it came from I do not know. It may have been multiple abscesses. I do not believe that it could have been an amebic abscess.

DR. HOLMES: Were the sinuses examined? It is possible that the pus was coming from the sinuses instead of the lung.

DR. MEANS: A patient does not cough up a cupful of foul sputum daily and have symptoms for twelve years from a sinus.

DR. HELEN PITTMAN: Sinuses feed the bronchi.

DR. MEANS: Yes; but there has to be something in the bronchus.

DR. PITTMAN: I think that another point that Dr. Holmes brought out, namely, whether anyone saw the sputum, is a good one.

DR. MEANS: Well, of course, the whole history may be false, but I have to accept the facts given.

DR. CASTLEMAN: Dr. Meigs, will you tell us about your impression?

DR. J. V. MEIGS: This woman's acute illness necessitated a night visit. It was thought to be an

acute surgical emergency. When I saw her she did not look so well as this record implies. She appeared extremely sick and was nauseated and vomiting; the white-cell count was 25,000, with 93 per cent neutrophils. She had definite spasm and tenderness in the right abdomen. I could not make a diagnosis, nor did I believe that she was sick enough to warrant immediate surgical operation.

DR. MEANS: Did you think that she had intestinal obstruction?

DR. MEIGS: No; I thought that she might have had a chronic rupture of some viscus. There was a mass on the right side. I could not feel the edge of the liver. All I knew was that we ought to get her some place where we could follow her closely. She was brought here. The next morning she looked better and the white-cell count had dropped. I thought that she had some disease connected with the liver. I asked Dr. Jones to see her. We thought that it was some sort of medical problem quite definitely connected with the liver. I did not believe that the pulmonary difficulties had anything to do with it. Dr. Richard H. Overholt had bronchoscoped her and found bronchiectasis. Dr. Jones carried on.

DR. JONES: By the time I saw the patient there was little in the chest except for a few rales, particularly at the right base. We all thought that she had a low-grade bronchiectasis to account for part of the clinical picture, but we did not believe that it had caused the symptoms that brought her to the hospital. She had a large mass, which Dr. Meigs and I both thought was probably a large liver. It was extremely tender for two weeks after admission to the hospital. We could not be certain whether the tenderness was along the hepatic border or underneath the edge of the liver. As she improved, with adequate hydration and rather intensive vitamin therapy for obvious avitaminosis, it became clear that the tender mass actually was liver. The one test that gave us a direct clue was the bromsulfalein test, with 40 per cent dye retention in the absence of jaundice. Dr. Meigs and I decided that the sensible thing to do was to sit tight until she got better and then make absolutely certain that there was no disease besides the intrahepatic disease. For that reason she was explored.

The patient was explored with the idea that she had a subacute inflammatory, possibly cirrhotic, process in the liver, not necessarily on an infectious basis. We did not expect to find anything outside the liver. We simply wanted to make certain.

DR. MEANS: The chief point of disagreement between Dr. Jones, who saw the patient and therefore had more information, and me is whether the process in the liver was acute or subacute. There is nothing in the abstract on which I could say that it was other than acute. I did have cirrhosis down here on my list of differential diagnoses but forgot to mention it. You have to think of it because it is a frequent liver disease producing a great variety of pictures and does produce pain and fever. There have been a number of such cases, I recall one in particular, that of a nurse who had acute pain and was rushed to the amphitheater and was operated on, only to find that she had a cirrhosis. Of course I shall have to agree that cirrhosis is a possibility.

CLINICAL DIAGNOSIS

Subacute hepatitis (? cirrhosis).

DR. MEANS'S DIAGNOSES

Acute infectious hepatitis (? multiple abscesses, ? cirrhosis).
Chronic bronchiectasis.
Avitaminosis (B complex).

ANATOMICAL DIAGNOSIS

Acute alcoholic hepatitis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At operation a large fatty liver was found, and biopsy showed the findings that have been described in acute alcoholic hepatitis. It was not actually a cirrhosis, because at this stage there is no actual fibrosis. The liver cells were filled with fat, and many showed the hyaline network described years ago by Dr. Frank B. Mallory.* This case showed it to an extreme degree, and around these areas there was a marked polymorphonuclear infiltration, which may have accounted for the elevated white-cell count. In the later stages of this condition there is a replacement of liver cells by connective tissue and a gradual decrease in the size of the liver to one perhaps a little larger than normal, but rarely smaller than normal.

DR. JONES: There was a real discrepancy in the history as regards the use of alcohol; I think that it is fair to say that the use of alcohol was not known to be excessive, but it may have been an important factor. Six months before entry — and this is not mentioned in the history — the patient had an episode that was clearly one of acute pellagra and that might have contributed to the development of liver disease when combined with alcohol and other unknown factors. The leukocytosis is not inconsistent with acute liver damage, even on a noninfectious basis — a point not generally recognized. I have seen a white-cell count as high as 35,000 with many immature cells, such as young myelocytes, in patients with rapidly progressing hepatic damage.

It is interesting to add that this patient has been extremely well since leaving the hospital and the liver has receded almost to the costal margin.

DR. MEANS: There was no definite history of alcoholism?

DR. MEIGS: No more than cocktail parties all last summer.

*Mallory, F. B. *The Principles of Pathologic Histology*. Philadelphia: W. B. Saunders Company, 1914. Pp. 504-508.

CASE 31032

Presentation of Case

A thirty-three-year-old married woman was admitted to the hospital with malaise and diffuse distress in the lower abdomen.

One week prior to admission the patient's expected menstrual period did not appear. Instead she noted only slight staining, accompanied by a feeling of general malaise and weakness. Two days later she passed a small amount of blood per vaginam. She also noted slight soreness in the lower abdomen; this had no definite localization but gradually became more pronounced. One day prior to entry she again passed a small amount of blood. Although she felt rather "warm," there were no chills or fever. Her appetite was poor. There was no nausea, vomiting or diarrhea. She had had a normal bowel movement on the morning of admission.

The patient had been pregnant nine times and had had seven children. The last miscarriage had occurred six years before admission. Her menstrual periods were apparently regular.

Physical examination revealed a well-developed and well-nourished woman. The heart and lungs were negative. The abdomen revealed generalized tenderness with slight spasm, most marked in the right lower quadrant. Peristalsis was normal. Pelvic examination revealed a slightly enlarged uterus in anterior position; it was very tender, especially on the right. The cervix was large and lacerated, with numerous nabothian cysts. A round, firm, exquisitely tender, golf-ball-sized mass was felt posteriorly.

The temperature was 99°F., the pulse 90, and the respirations 20. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood showed a white-cell count of 11,000. The urine was negative.

A laparotomy was immediately performed.

Differential Diagnosis

Dr. John L. Newell: This woman of childbearing age had missed one period, and in starting to discuss the case we must first try to determine whether she was pregnant. She had amenorrhea but no history of nausea. The uterus was slightly enlarged. No mention is made of any softening of the cervix. It was too early to get a definite Hegar's sign, but there should be softening, unless it was masked by scarring subsequent to lacerations at previous childbirths. I think it is fair to assume, however, that she had an early pregnancy and that, with this irregular spotting, there was a threatened abortion. Whether the pregnancy was intrauterine or extrauterine is the next question to decide. The uterus is described as being enlarged and tender. The tenderness puzzles me somewhat because, unless there had been an attempt at a criminal abortion, I cannot interpret it. What is meant I believe is that manipulation of the uterus, rather than bimanual pressure on the uterus itself, caused pain.

Dr. Benjamin Castleman: The note says that the uterus was "very tender."

Dr. Newell: I do not remember seeing either an intrauterine or an extrauterine abortion in which the uterus itself was tender. Tenderness in the right vault is to be expected if it was an extrauterine pregnancy.

The next thing that comes to mind is the firm, — and I emphasize the word "firm," — exquisitely tender mass, about 4 cm. in diameter, in the pouch of Douglas. If she had an extrauterine pregnancy and had had an incomplete tubal abortion, having pushed the ovum into the peritoneal cavity, the mass should not be that large, and at this stage of pregnancy it should not be so firm as described. I shall return to that later.

The abdominal findings are interesting. She had a history of pain, which became severer over a period of days. She had also tenderness, chiefly localized in the right lower quadrant. This, of course, is consistent with an incomplete tubal abortion, and that is also true for the temperature, pulse, blood pressure and leukocytosis. The main point in my mind against an ectopic pregnancy is this mass. I believe that she had a twisted cyst of the right ovary. Whether the cause of the abortion was the fact that the corpus luteum happened to be in the right ovary, I do not know; that would be a perfectly logical conclusion.

Dr. Fred A. Simmons, Jr.: According to our experience in the Emergency Ward, the presence of a mass in the pelvis that is exquisitely tender is definite evidence of tubal pregnancy. I believe that this patient did have a tubal pregnancy.

Dr. Edward Hamlin, Jr.: Would it not be unusual for the mass to be described as round, firm and golf-ball-sized? The description alone, if it is accurate, argues against tubal pregnancy; such a mass is usually indefinite with the amount of pressure that one can use and is seldom firm.

Dr. Newell: This ovum was only three weeks of age. If it had been aborted into the pouch of Douglas, the mass might be as large as a golf ball because of surrounding blood clot, but it should not be firm and hard.

Dr. Francis M. Ingersoll: I agree that it seems much more like a cyst that had twisted than a tubal pregnancy; she may have had an intrauterine pregnancy that was ready to abort.

Clinical Diagnosis

Tubal pregnancy.

Dr. Newell's Diagnoses

Cyst of right ovary, with torsion.
Probable intrauterine pregnancy.

Anatomical Diagnosis

Acute salpingo-oöphoritis.

Pathological Discussion

Dr. Castleman: I am sorry that the surgeon who operated on this patient is not here. At operation he found a slightly enlarged uterus; the right tube was thick, red and reflected on itself, so that the fimbriated end lay in the posterior cul-de-sac and was held there by adhesions. The left tube was also slightly reddened but normal in size and shape. The right ovary was moderately enlarged, firm and intimately connected with the enlarged right tube. The tube and ovary were removed.

The preoperative and postoperative diagnoses were ectopic pregnancy, but microscopic examination showed no evidence of pregnancy. The tube was markedly edematous and filled with pus. It was one of the most acutely inflamed tubes that we have seen for a long time, but of course they are usually not removed in the acute stage. There was acute inflammatory disease of the pelvis, which had involved the right tube and ovary and, to a lesser degree, the left tube. There was probably also an acute endometritis, which perhaps accounted for the slight increase in the size of the uterus.

Dr. Simmons: Was she pregnant?

Dr. Castleman: No; a Friedman test done after operation was negative, which ruled out an intrauterine pregnancy. I do not believe that pregnancy could have occurred in the presence of such a pyosalpinx.

Dr. Simmons: Is it not true that you frequently receive specimens from patients who clinically have proved tubal pregnancies in which you do not find decidua or villi?

Dr. Castleman: In such cases the tubes are filled with blood and there is no acute infection in the wall of the tube. In this case there was inflammation in the wall of the tube, frank pus within it, and fibrin on its surface. There is no doubt about the diagnosis.

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THE SHORTAGE OF NURSES

Releases appearing almost daily in the newspapers emphasize the shortage of trained nurses in the armed forces and make an appeal for enlistment of those who are properly qualified. On the other hand, such enlistment means further depletion in the ranks of those who are now employed in civilian communities — a fact that is bound to result in an even greater curtailment of nursing service in hospitals and homes than exists at the moment. To supplement the nursing care available to civilians the American Red Cross has successfully instituted two types of training — that of nurse's aides and that designed for instruction in the care of the sick in the home.

The former activity has been eminently successful. Indeed, many hospitals have testified that without the skilled help of these volunteers it would have been impossible to maintain hospital service at an efficiency level.

The training in home nursing comprises a series of twelve two-hour lessons in which the students learn to recognize certain signs of illness, to apply simple remedies, to take and record the temperature and pulse, to dispose of dangerous excreta, to give an enema and so forth. Students practice moving the patient and making the bed without unduly disturbing him, they learn how to prepare tasty meals, and they are encouraged to improvise simple equipment designed for the comfort of the patient. Furthermore, keeping the family well and avoiding the complications arising out of neglect through daily, watchful care are impressed on the student. Unsung and ununiformed, the home-nursing student becomes the monitor of health in the home and the doctor's able collaborator when sickness strikes. She does not make a diagnosis, she keeps calm in time of crisis, and she appreciates good medical service. To deal with understanding people who are not utterly ignorant of simple procedures and who can be relied on to carry out orders intelligently is of great assistance to the doctor.

Since July 1, 1944, seventy-five home-nursing classes have been completed in Massachusetts, and two hundred and thirty-five classes are now in session. Approximately three hundred registered graduate nurses, specially trained as instructors, are authorized to teach the classes, which they do at no little sacrifice. A textbook supplements the course and remains the property of the trainee.

The practicing physician can do much to encourage women to enroll in home-nursing classes. The family of each patient who is being treated in the home should be questioned whether someone is a certificate holder. If no one has taken the course, this often prompts the mother or sister, or even the father, to enroll in the next class at the local Red Cross chapter. The physician can also support this enterprise by suggesting methods and means for improving the course that is given in his community. No one is more acutely aware of the shortage of nurses than is the physician, and the American Red Cross deserves his enthusiastic and whole-hearted support.

V. D.

THE war against V. D. is going well. Turner[1] in reporting on the control of these diseases since 1940 points out that the yearly time lost from these infections in the United States Army has been reduced from 1278 days per 1000 men in 1940 to 368 days in 1943. The Army data also show that the V. D. morbidity rate is below the preceding peace level and half that of World War I.[2] In civilian life a review of the figures for all states for 1943–1944 shows 100,000 fewer cases of syphilis than previously; in only thirteen states were there more cases than before, and in most of these states the increase was slight.[3]

Much credit for these excellent results among military personnel must be given to the appointment of V. D. C. (venereal-disease-control) officers in the Army and in the United States Public Health Service. Their conscientious efforts at various stations deserve every commendation that can be bestowed. Much has been attained by applying the principles of preventive medicine to these diseases. Such a program has been well outlined in a recent number of *Lancet* by Gordon.[4] It is to be hoped that this program can be carried over into civilian life in the postwar period.

These V. D. C. officers have also had the advantage of the apparently improved therapeutic measures that have been developed in the last four or five years. The progress report in this issue of the *Journal* reviews these new methods of treatment — the use of penicillin and the sulfonamides, the intensive use of arsenicals and their combination with fever therapy and so forth. This report also strongly emphasizes the need for caution in universally adopting these procedures until they have been found to be safe and have been proved to produce, in the long run, as good or better end results than the present-day accepted methods of treatment have accomplished.

Many other matters in connection with these diseases need further thought and discussion. The matter of juvenile delinquency has been found to be tied closely to this problem, and every agency should be mobilized to aid in the solution of reaching the family and the small community. Education of the civilian population in matters pertaining to these diseases has been stressed and much has been done, but further effort is needed. Demobilization will bring its problems. Will the venereally infected veteran be discharged before cure to carry the infection back to civilians, or will he be held and paid as a soldier until cured? Will the experience of the V. D. C. officers in this field be put to use in civilian life to lessen further the incidence of these diseases? Time only can answer these and other questions.

With the epidemiologic principles set forth by Gordon and the experience gained in the war, with adequate regulations and their enforcement regarding contagious disease and with the rational use of the new therapeutic procedures, the demobilized V. D. C. officer can contribute greatly to a further decrease in the incidence of venereal disease.

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MASSACHUSETTS MEDICAL SOCIETY

STATED MEETING OF THE COUNCIL

A stated meeting of the Council of the Massachusetts Medical Society will be held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, February 7, 1945, at 10:30 a.m.

Business:

1. Call to order at 10:30 a.m.
2. Presentation of record of meeting held October 4, 1944, as published in *The New England Journal of Medicine*, issue of December 21, 1944.
3. Reports of standing and special committees.
4. Appointment of delegates:
   (a) To the House of Delegates, American Medical Association, for two years from June 1, 1945.
   (b) To the annual meetings of the five New England state medical societies in 1945.
   (c) To the Annual Congress of the American Medical Association on Medical Education and Licensure at the Palmer House, Chicago, February 12 and 13, 1945.
5. Such other business as may lawfully come before this meeting.

MICHAEL A. TIGHE, M.D., *Secretary*

DEATHS

MAHONEY — John L. Mahoney, M.D., formerly of Boston, died January 2 at St. Petersburg, Florida. He was in his seventy-third year.

Dr. Mahoney received his degree from Boston University School of Medicine in 1898.

WIGGIN — William I. Wiggin, M.D., of Lowell, died January 3. He was in his sixty-sixth year.

Dr. Wiggin received his degree from McGill University Medical School in 1901. During World War I he served overseas for eighteen months with a Red Cross field unit. He taught otolaryngology at Harvard Medical School from 1919 until his retirement a few years ago. During the same period he served as staff surgeon at the Massachusetts Eye and Ear Infirmary. He had also been a member of the Lowell General Hospital staff for many years. He was a fellow of the American College of Surgeons and the American Medical Association, and a member of the American Board of Otolaryngology, the American Academy of Ophthalmology and Otolaryngology, and the New England Otological and Laryngological Society. At the time of his death, he was vice-president of the Middlesex North District Medical Society.

His widow and his mother survive.

CORRESPONDENCE

TREATMENT OF THE COMMON COLD

To the Editor: In the April, 1944, issue of the *Journal of the Maine Medical Association* there appeared an article by me which was a review of outstanding work pertaining to the common cold. The review was made because of the fact that a number of patients had divulged that they had received "cold serums" and other useless forms of medication that, on the whole, seemed to be perhaps more harmful than good.

The onset of the common cold — the virus stage — is characterized by sneezing, watery discharge and stuffiness of the nose, with a subnormal or normal temperature. Influenza, on the other hand, has a sudden onset with fever, headache and neuromuscular or gastrointestinal manifestations.

During the virus stage of the common cold, which lasts for three or four days, immediate and proper treatment can abort the secondary phase of this ailment.

One must avoid drying, mentholated, creamy or oily nose medication, cathartics and alcohol. Equally useless, in my mind, are the vitamins (in the otherwise healthy person), sulfonamides, soda, aspirin, calcium and iodine, liver oil, amytal, ephedrine, atropine, quinine and like drugs.

The crux of the treatment for the virus phase of the common cold is in the intelligent use of the hot bath and medication with the opium derivatives, codeine and papaverine. Such treatment has never failed to abort the first stage of the common cold in any of my patients who followed directions explicitly.

Copavin, which is a commercial preparation containing ¼ gr. each of codeine and papaverine, is given, the dosage being one tablet (or capsule) after meals and two at bedtime or one tablet every three hours and two at bedtime. The dosage is regulated according to the severity of the symptoms and to the size of the patient. If the symptoms are severe, two tablets may be given for the first and second doses and three at bedtime. For children the dosage is, of course, regulated according to size. The codeine-papaverine combination was conceived by Diehl and his co-workers, who observed that chronic users of opium and its derivatives were remarkably free from the common cold.

The hot-bath regime must be explained to the patient. The tub should be half full of *hot* water, and the body should be kept well immersed until perspiration occurs on the head (debilitated patients should not, of course, be submitted to this). From the bath the patient goes immediately to a warmed bed and remains there two or three hours in a well-aired room.

If this treatment is performed during the early stage of the common cold the secondary stage, with its week or two of distress, can be entirely eliminated.

LLOYD H. BERRIE, M.D.

Caribou, Maine

BOOK REVIEWS

The Romance of Medicine: The story of the evolution of medicine from occult practices and primitive times. By Benjamin L. Gordon, M.D. 8°, cloth, 624 pp., with 145 illustrations. Philadelphia: F. A. Davis Company, 1944. $5.00.

This volume is not a history of medicine in the conventional biographic pattern; rather, it is a series of philosophic essays on the evolution of medicine from the standpoint of a number of its principal problems in primitive time — animism, reproduction, heredity, physiology, disease, demonology, witchcraft, hysteria, the evil eye, astrology, symbolism, superstition, scapegoatism, signature, biologic products, hydrotherapy, psychotherapy, medical ethics and immortality. Under each of these subjects the author surveys the field from prehistoric to modern time, with a wealth of scholarly allusion, quotation and reference. Everything in modern medicine has derived, often in devious ways, from the earliest past. That is what to him constitutes its romance.

The book contains excellent illustrations, many of which are unfamiliar. The footnotes, which afford a compendium of strange information and references in addition to those of the text, are extremely valuable.

The more one contemplates the eccentricities of the past, the less one wonders at those of the present. No book is quite like this, unless it be Dr. Howard W. Haggard's *Devils, Drugs and Doctors* of fifteen years ago. Dr. Gordon's essays are wider-ranging, but all are from the same point of view. It is unfortunate that so excellent a work is marred by so many obvious misprints; the book is, nevertheless, a worthy achievement of scholarship.

The Dental Treatment of Maxillo-Facial Injuries: With supplementary material on cases and techniques. By W. Kelsey Fry, M.C., M.R.C.S., L.R.C.P., L.D.S., R.C.S. (Eng.), P. Rae Shepherd, L.D.S., R.C.S. (Eng.), Alan C. McLeod, D.D.S. (Penn.), B.Sc. (dent., Toronto), L.D.S., R.C.S. (Eng.), and Gilbert J. Parfitt, M.R.C.S., L.R.C.P., L.D.S., R.C.S. (Eng.). With foreword by Professor F. R. Fraser, M.D., F.R.C.P., and a section on fractures of the middle third of the face by A. H. McIndoe, M.S., F.R.C.S., F.A.C.S. 8°, cloth, 434 pp., illustrated. Philadelphia: J. B. Lippincott Company, 1944. $6.50.

The surgical treatment of wounds has made great progress in the last thirty years. This branch of surgery began in World War I, but progress slowed down between 1918 and 1939. In the present war it is, of necessity, again progressing and has made its greatest advance in the field of facial injuries.

Fry and his colleagues have presented the knowledge accumulated during the last thirty years with clarity and intelligence. This book originally appeared in England and was published in two separate volumes, but the American publishers have wisely combined the material into a single volume.

The first half of the book presents all phases of maxillofacial injury, including the treatment of soft-tissue injuries as well as bony injuries, with detailed descriptions of the methods of fixation, all illustrated with excellent photographs and diagrams.

The second half of the book is chiefly devoted to case studies and technic. The outstanding chapters in this section are those on pathology and surgery, illustrated with colored photomicrographs. There is also a chapter on fractures of the middle third of the face, which includes fractures of the maxillary, nasal and malar bones. Several case histories are presented, each with remarks and an analysis of the method of treatment employed.

The title suggests that this book deals primarily with the dental treatment of facial injuries, that is, with the treatment by dental surgeons. This inference is partly true, but the book also presents instructive chapters for plastic and general surgeons who may be called to treat facial injuries.

In reading this book one is impressed with the central idea: in treating maxillofacial injuries, especially in combat areas, there must be intelligent co-operation and co-ordination by the dental and the plastic surgeons. Emphasis is also placed on the importance of specialized centers for the treatment of these casualties, where the teamwork that is essential for the best results can be obtained.

Technique in Trauma: Planned timing in the treatment of wounds including burns. From the Montreal General Hospital and McGill University. By Fraser B. Gurd, M.D., C.M.; and F. Douglas Ackman, M.D., C.M. In collaboration with John W. Gerrie, M.D., C.M., Edward S. Mills, M.D., C.M., Joseph E. Pritchard, M.D., and Frederick Smith, M.D. Preface by John S. Lockwood, M.D. With commentary by Ralph R. Fitzgerald, M.D., C.M. 4°, cloth, 68 pp., with 3 plates, 17 figures, 5 tables and 3 charts. Philadelphia: J. B. Lippincott Company, 1944. $2.00.

This book consists of three papers published within the last two years, together with an introduction and a commentary that represent new material. These papers outline the detailed directions now being used in the Montreal General Hospital, treatment being based on the use of the most advanced and modern concepts that are now current in the surgical world. They therefore make available to the practitioner and student, in easily assimilable form, methods of treatment that have been safely and successfully used. Anyone who is occasionally or frequently confronted with decisions in the care of serious burns, extensive soft-part injuries or compound fractures can well afford to buy and give careful thought to the contents of this book.

Above all, it stresses that no individual can give adequate treatment to these cases but that carefully trained teams are necessary. This has been a universal experience in the last few years, but the organization of the necessary teamwork has seldom been discussed.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Infants without Families: The case for and against residential nurseries. By Anna Freud; and Dorothy Burlingham. 12°, cloth, 128 pp. New York: International University Press, 1944. $2.00.

This monograph deals with the care of homeless and parentless children, made so by the exigencies of war. It is based on the authors' experience at the Hempstead Nurseries in England. An attempt has been made to evaluate the advantages and disadvantages of institutional life at different phases of the infant's development. The text is divided into a number of chapters having to do with the aspects of development between birth and two years, early relations between institutional infants, introduction of the mother-relation into the nursery life, some aspects of instinctual satisfaction and frustration in family and nursery life, the role of the father in the residential nursery and the growth of the child's personality under nursery conditions. The authors conclude that institutional nurseries offer excellent opportunities for detailed and unbroken observation of child development but agree that the continuance of such nurseries after the war will be decided probably by social and economic needs and not on the basis of psychologic requirements. The primary objective of the book is to discuss the questions: Should residential nurseries be maintained and, if so, can they be changed so as not to produce the so-called "institutional child"?

Man Does Not Stand Alone. By A. Cressy Morrison. 12°, cloth, 107 pp. New York: Fleming H. Revell Company, 1944. $1.25.

This small book attempts a review of the scientific evidence of the existence of a supreme intelligence and is written as a challenge to Julian Huxley's *Man Stands Alone*, in which Mr. Huxley states that he does not believe in God or gods.

Bailey's Textbook of Histology. Revised by Philip E. Smith, Ph.D., professor of anatomy, College of Physicians and Surgeons, Columbia University; and Wilfred M. Copenhaver, Ph.D., associate professor of anatomy, College of Physicians and Surgeons, Columbia University. With the assistance of Aura E. Severinghaus, Ph.D., associate professor of anatomy, College of Physicians and Surgeons, Columbia University, and Charles M. Goss, M.D., professor of anatomy, University of Alabama Medical School. Eleventh edition. 8°, cloth, 786 pp., with 470 illustrations. Baltimore: The Williams and Wilkins Company, 1944. $6.00.

This edition of an authoritative teaching text, first published in 1904, has been thoroughly revised. The primary objective of providing a text for first-year medical students has been adhered to as in previous editions. The chapter on the female reproductive system has been amplified by the addition of a section on the placenta. The text throughout the book has been brought up to date and in places has been extended or clarified. Many new figures in color and halftone have been introduced throughout the book. Lists of carefully selected bibliographic references are appended to each chapter.

Heart Disease. By Paul D. White, M.D., lecturer in medicine, Harvard Medical School, and physician, Massachusetts General Hospital, Boston. Third edition, completely revised and reset. 8°, cloth, 1025 pp., with 138 illustrations. New York: The Macmillan Company, 1944. $9.00.

This standard treatise has been thoroughly revised and brought up to date. An important addition is a chapter on the range of the normal heart. New material added includes phonocardiography, precordial leads, ligation of the patent ductus arteriosus, treatment of subacute bacterial endocarditis, splanchnic resection for hypertension, intracardiac thrombosis, pulmonary embolism and the heart in gastrointestinal diseases. There is also a new section on heart disease in military service. Many of the historical references that appeared in the first edition and were omitted in the second have now been replaced, owing to a demand from the readers of the book. New references to articles of importance appearing during 1937–1943 have been added after each chapter, whereas many of the references of current interest in the years 1931–1936 have been omitted. In order to obtain a complete bibliography one must consult the editions of 1931 and 1937. A number of illustrations have been added to the text.

Fundamentals of Internal Medicine. By Wallace M. Yater, M.D., M.S. (med.), professor of medicine and director of the Department of Medicine, Georgetown University School of Medicine, physician-in-chief, Georgetown University Hospital, and physician-in-chief, Gallinger Municipal Hospital, Washington, D. C. Second edition. 8°, cloth, 1204 pp., with 275 illustrations. New York: D. Appleton–Century Company, Incorporated, 1944. $10.00.

The second edition of this book has been revised to conform to war conditions. New material of interest to the military internist has been added, including medical problems incidental to flying, immersion foot, blast injuries, effects of chemical warfare, war neuroses and tropical medicine. Many other subjects have been added or revised, including blood-typing, liver-function tests and a preliminary evaluation of penicillin. Three new sections have been written entitled "Symptomatic and Supportive Treatment," "Clinical Values and Useful Tables" and "The Physician Himself." A more comprehensive index has been made, and additional illustrations have been inserted in the text. The objective of this book is to include in one volume all the clinical subjects that an internist may encounter in his daily work.

The Electrocardiogram: Its interpretation and clinical application. By Louis H. Sigler, M.D., attending cardiologist and chief of the Cardiac Clinic, Coney Island and Harbor hospitals, New York. 8°, cloth, 403 pp., with 203 illustrations. New York: Grune and Stratton, Incorporated, 1944. $7.50.

The objective of this book is to present in a simple but comprehensive manner all that relates to the electrocardiogram and its practical application to cardiology. The work is well illustrated with figures comprising nearly four hundred electrocardiograms. The book is divided into twenty-five chapters beginning with the biological and physical foundations of the electrocardiograph, its recording and the classification of electrocardiograms, followed by chapters on the various cardiac disorders.

Rehabilitation, Re-education and Remedial Exercises. By Olive F. Guthrie Smith, M.B.E., C.S.M.M.G., T.M.G., principal of the Swedish Institute, London, and director of

the Physical Exercise Department, St. Mary's Hospital. With a foreword by Lord Horder, G.C.V.O., M.D., F.R.C.P. 8°, cloth, 424 pp., with 273 illustrations. Baltimore: The Williams and Wilkins Company, 1943. $6.00.

This book is devoted primarily to a discussion of remedial exercises in various orthopedic conditions, with emphasis on the suspension methods of the author.

X-Ray Examination of the Stomach: A description of the roentgenologic anatomy, physiology and pathology of the esophagus, stomach and duodenum. By Frederic E. Templeton, M.D., head of the Department of Roentgenology, The Cleveland Clinic. 8°, cloth, 516 pp., with 297 illustrations. Chicago: The University of Chicago Press, 1944. $10.00.

This monograph is devoted to an intensive study of the upper digestive tract by the x-ray. It includes a presentation of modern, roentgenologic methods and their use and interpretation, together with the detailed consideration of the normal and abnormal manifestations encountered in the stomach, esophagus and duodenum, with careful, differential diagnosis. The filming fluoroscope is described and discussed. The work is well illustrated and printed on heavy paper in a legible type.

Insulin Shock Therapy. 8°, paper, 97 pp., with 13 tables. New York: Temporary Commission on State Hospital Problems, 1944. Available, without cost, on application.

The commission recommends that insulin-shock therapy for dementia praecox be made available in all the state hospitals for the insane in New York. The recommendation is based on the results of an intensive study of 1128 dementia-praecox patients treated with insulin shock at the Brooklyn State Hospital in five and a half years and a comparable group of 876 patients admitted to the state hospitals in the metropolitan area who did not receive that form of treatment. The commission found that insulin-treated patients did better in all respects than a group not so treated. More patients left the hospital after a shorter stay, and a larger number were living usefully at home. It was also found that over half the institutional population of mental hospitals was made up of dementia-praecox cases. The reports showed great direct savings in hospital days and in the cost of food and clothing and undetermined indirect savings in maintenance costs and ultimately in construction costs. The commission was appointed in November, 1940, and made a progress report in November, 1942, at which time it recommended the extension of shock therapy, as well as increasing the number of patients placed on parole or in family care. It stated that increased effort in these directions had not only halted the rate of increase of patients in state hospitals but that during a four-month period in 1942 the long-standing average increase of about 2400 patients had given place to a decrease of 78. This was the first such reversal in fifty years of state care of the insane. The commission concludes that insulin-shock therapy produces substantially better results in the treatment of dementia praecox than those obtained when insulin is not administered. What is more striking, good results were obtained even in those cases in which the prognosis without insulin is usually doubtful, such as patients in the older age groups, those whose illnesses have a duration of more than a year and those with a gradual onset.

New and Nonofficial Remedies, 1944. Issued under the direction and supervision of the Council on Pharmacy and Chemistry, American Medical Association. 12°, cloth, 778 pp. Chicago: American Medical Association, 1944. $1.50.

The current volume of *New and Nonofficial Remedies* reflects two important and forward-looking decisions of the Council, namely, to use the metric system exclusively in all its publications and to consider for acceptance contraceptive preparations offered for use as prescribed by physicians.

The chapter on contraceptives is quite comprehensive, and the Council has thus far accepted certain contraceptive jellies and creams, diaphragms, diaphragm inserts, syringe applicators and fitting rings.

A number of new preparations are described. Certain general articles have been revised to bring them up to date, and more or less important revisions have been made in other chapters.

Surgical Disorders of the Chest: Diagnosis and treatment. By J. K. Donaldson, M.D., associate professor of surgery and in charge of thoracic surgery, University of Arkansas School of Medicine, and member of surgical staff, St. Vincent's Infirmary, and visiting staff, Baptist Hospital, Little Rock, Arkansas. 8°, cloth, 364 pp., with 127 illustrations. Philadelphia: Lea and Febiger, 1944. $6.50.

This new work on thoracic surgery has been written primarily for general practitioners, general surgeons and students. It contains in a simple form the advances made in the field of chest surgery during the past decade. In line with this objective, controversial discussions, long statistical and historical reviews, unnecessary detail and long bibliographies have been omitted. Some discussion pertaining to war injuries has been included, although the author believes that the fundamental problems, with a few exceptions, are the same in both war and civilian injuries of the chest.

The Art of Anaesthesia. By Paluel J. Flagg, M.D., visiting anesthetist to Manhattan Eye and Ear Hospital, consulting anesthetist to St. Vincent's Hospital, New York, consulting anesthetist to the Woman's Hospital, Sea View Hospital, Jamaica Hospital, Mount Vernon Hospital, Flushing Hospital, Mary Immaculate Hospital, St. Mary's Hospital (Far Rockaway) and Nassau Hospital, Long Island. Seventh edition. 8°, cloth, 517 pp., with 166 illustrations. Philadelphia: J. B. Lippincott Company, 1944. $6.00.

Five years have elapsed since the sixth edition of this standard text was published. During this period much progress has been made in the field of anesthesia. This edition discusses thoroughly the pros and cons of military anesthesia, as well as the newer developments in the field of anesthesia.

The Gastro-Intestinal Tract: A handbook of roentgen diagnosis. By Fred J. Hodges, M.D., professor of roentgenology, University of Michigan Medical School. 8°, cloth, 320 pp., with 130 plates. Chicago: The Year Book Publishers, Incorporated, 1944. $5.50.

This manual consists of a large number of reproductions of x-ray films, with running descriptions of each.

The Analysis and Interpretation of Symptoms. Edited by Cyril M. MacBryde, M.D. 8°, cloth, 301 pp., illustrated. Philadelphia: J. B. Lippincott Company, 1944. $9.00.

This symposium by ten specialists gives the basis for analysis and interpretation of some of the common symptoms found in patients. Emphasis is placed on the pathologic physiology of symptoms, whereas their correlation with other symptoms and with physical and laboratory evidence is considered as important but secondary in the diagnostic method.

NOTICES

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held on Monday, January 29, at 8:15 p.m., at the Boston Medical Library.

PROGRAM

Echinococcal Heart Disease. Drs. Lewis Dexter and John Peters.

Some Clinical Effects of Cytochrome C in Anoxia. Drs. Samuel Proger, D. Decaneas and Gerhardt Schmidt.

Studies on Experimental Pulmonary Edema. Drs. A. A. Luisada and S. J. Sarnoff.

Insomnia Due to Unrecognized Left Ventricular Failure. Drs. Edwin Wheeler, Conger Williams, and Paul D. White.

Interested physicians and medical students are cordially invited to attend.

(*Notices continued on page xv*)

NOTICES (*Continued from page 94*)

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, January 25

Friday, January 26

*9:00–10:00 a.m. The Treatment of Thyrotoxicosis with Anti-thyroid Drugs. Dr. R. Williams. Joseph H. Pratt Diagnostic Hospital.

10:50 a.m. Use of X-Ray and Radium in Dermatology. Dr. Bernard Appel. (Postgraduate clinic in dermatology and syphilis.) Dowling Amphitheater, Boston City Hospital.

Saturday, January 27

*10:00 a.m.–12:00 m. Medical staff rounds. Peter Bent Brigham Hospital.

Monday, January 29

*12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

Tuesday, January 30

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

Wednesday, January 31

*9:00–10:00 a.m. A Recent Advance in Dermatological Therapy. Dr. Francis M. Thurmon. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

7:15 p.m. Graduate seminar in pediatrics. Children's Medical Service. Amphitheater 3A, Massachusetts General Hospital.

*Open to the medical profession.

January 19. New England Roentgen Ray Society. Page 62, issue of January 11.

January 20 and 21. Forum on Allergy. Page 638, issue of November 2.

January 23. Greater Boston Medical Society. Page 62, issue of January 11.

January 29. New England Heart Association. Page 94.

February 3. American Board of Obstetrics and Gynecology. Page 696, issue of November 16.

February 8. Surgery Connected with the Liver and Pancreas. Dr. Joseph Tartakoff. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

February 11. National Conference on Medical Service. Page 30, issue of January 4.

February 19. American Board of Internal Medicine. Page 436, issue of September 21.

May 22–24. Hotel Statler, Boston. Annual meeting of the Massachusetts Medical Society.

September 17. American Public Health Association. Page 752, issue of November 30.

District Medical Societies

PLYMOUTH

February 15. Jordan Hospital, Plymouth.
March 15. Goddard Hospital, Brockton.
April 26. Toll House, Whitman.
May 17. Lakeville Sanatorium, Lakeville.

All meetings will be held at 11 a.m.

WORCESTER

February 14. Worcester State Hospital.
March 14. Worcester Memorial Hospital.
April 11. Hahnemann Hospital, Worcester.
May 9. Annual meeting.

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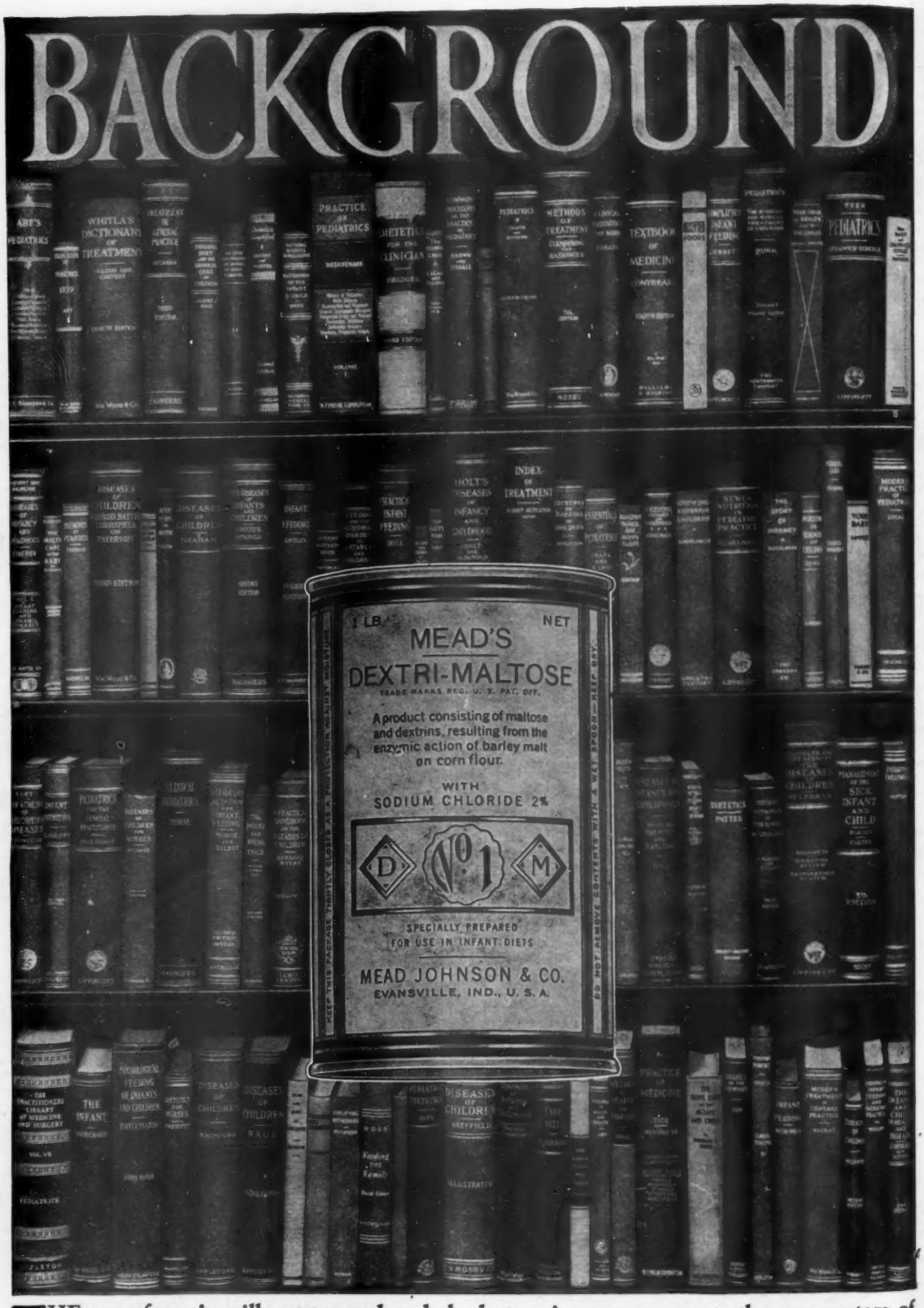
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